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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.—Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. — Publisher.

ENTHALPY OF FORMATION OF STRONTIUM PHOSPHIDE

S. A. Shchukarev, M. P. Morozova and Kan Kho Yn

The system strontium-phosphorus has not been studied up to now. The preliminary studies made by us show that not a single compound exists in it; the existence of the compound Sr_3P_2 is not open to doubt, since a substance of this composition reacts with dilute hydrochloric acid to form only the gaseous phosphorus hydride PH_3.

We prepared strontium phosphide, Sr_3P_2, by reacting phosphorus with metallic strontium. The two substances, taken in the ratio corresponding to the formula Sr_3P_2, were placed separately in two boats in a glass tube, which after good evacuation was sealed.

Heating of the tube to 400-450° caused all of the phosphorus to be absorbed by the strontium. After this the obtained phosphide was annealed for a long time in a quartz tube at 900-1000°. The strontium phosphide prepared in this manner is a finely crystalline dark-gray powder, exceedingly sensitive to atmospheric moisture.

The analysis results of the synthesized preparations are given below.

Found %: Sr 80.63, 80.52, 80.77, 80.70; P 18.93, 18.87, 18.67, 19.02, Sr_3P_2.
Calculated %: Sr 80.92; P 19.08.

The enthalpy of formation of strontium phosphide was established from the value of the enthalpy for the reaction of Sr_3P_2 with dilute hydrochloric acid. The chamber of the calorimeter, in which this reaction was run, was first blown with hydrogen to exclude the possibility of phosphine oxidation. The method of running the calorimetric determinations had been described by us earlier [1].

We found the following values for the enthalpy of this process: −235.4, −233.8, −237.3, −237.5, −235.4, i.e. on the average −235.9 ± 2 kcal./gram-formula.

$$Sr_3P_{2\,cryst} + 6HCl_{soln} = 3SrCl_{2\,soln} + 2PH_{3\,gas} + 235.9 \pm 2 \text{ kcal.}$$

In combination with the known values for the enthalpies of formation of hydrogen chloride, strontium chloride and phosphine and the values of the enthalpies for the solution of hydrogen chloride and strontium chloride, a value of −160.03 ± 2 kcal./gram-formula is correspondingly obtained for the enthalpy of formation of strontium phosphide:

$$3Sr_{cryst} + 2P_{cryst} = Sr_3P_{2\,cryst} + 160.03 \pm 2 \text{ kcal.}$$

The enthalpy of formation of strontium nitride is equal to −92.2 kcal./gram-formula, the enthalpy of formation of strontium stibnide, Sr_3Sb_2, −134.7 kcal./gram-formula, and of strontium bismuthide, Sr_3Bi_2, correspondingly 126.8 kcal./gram-formula. As a result, the values for the enthalpies of formation of compounds of strontium with phosphorus, antimony and bismuth lie quite close to each other.

A completely different course is observed for the compounds of magnesium with the elements of the main subgroup of Group V: the enthalpies of formation of Mg_3P_2, Mg_3Sb_2 and Mg_3Bi_2 are (in kcal./gram-formula) respectively −119, −80 and −40, i.e. the replacement of magnesium in the compounds with phosphorus, antimony and bismuth by strontium leads to a considerable smoothing out of the differences in the heats of formation of the compounds following one after the other in the periodic system.

SUMMARY

By determining the enthalpy for the reaction of strontium phosphide with dilute hydrochloric acid the enthalpy of formation of strontium phosphide was found to be equal to −160.03± 2 kcal./gram-formula.

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ENTHALPY OF FORMATION OF LITHIUM AND BARIUM BISMUTHIDES

S. A. Shchukarev, M. P. Morozova, Kan Kho Yn and V. T. Sharov

Lithium bismuthide, Li_3Bi, was prepared by fusing the components, taken in stoichiometric ratio, in a hermetically sealed steel crucible at a temperature up to 1200°. The compound prepared in this manner is a coarsely crystalline dark-green substance.

The reaction of Li_3Bi with dilute hydrochloric acid proceeds very vigorously by the equation:

$$Li_3Bi_{cryst} + 3HCl_{soln} = 3LiCl_{soln} + Bi_{cryst} + \tfrac{3}{2}H_{2\,gas}.$$

The enthalpy values of this process obtained by us for various alloys are summarized in Table 1 (the method used to make the calorimetric determinations was described earlier [1]).

On the average the enthalpy of process (1) can be taken as equal to -160.2 ± 0.6 kcal./gram-formula.

In combination with the values for the enthalpies of formation and solution of hydrogen chloride and lithium chloride [2] a value of -39.5 ± 0.5 kcal./gram-formula is obtained for the enthalpy of formation of lithium bismuthide:

$$3Li_{cryst} + Bi_{cryst} = Li_3Bi_{cryst} + 39.5\pm 0.5 \text{ kcal.}$$

A different value had been proposed earlier for the enthalpy of formation of lithium bismuthide, and specifically -55.5 ± 3 kcal./gram-formula [3]. This value was found by the method of directly determining the heat of mixing of molten bismuth with metallic lithium. In its time this method was used to determine the enthalpies of formation of many intermetallic compounds; however, apparently almost always these data were not sufficiently reliable. The method of directly mixing the components frequently leads to errors in connection with the incomplete reaction of the two metals, which is due to the extremely short time that the metals are found at temperatures at which the reaction process between them is not frozen. This was shown in a series of studies, executed at the Chair of Inorganic Chemistry of the Leningrad State University [4, 5].

Another source of error in the method of directly determining the heat of mixing apparently consists in the fact that it is difficult to avoid partial oxidation of such active metals as lithium, barium, etc. Evidently, it is specifically this circumstance that is responsible for the fact that the direct mixing method at times gives high (in absolute value) values for the enthalpy of formation of some compounds of lithium and barium (as a rule, for the reason indicated earlier, lower values are obtained for the heats of formation of the compounds of the less active metals).

We also prepared barium bismuthide, Ba_3Bi_2, by the fusion of bismuth with barium, obtained by the method of high-vacuum aluminothermy, in a steel crucible at a temperature close to 1100°.

The enthalpy values for the reaction of barium bismuthide with dilute hydrochloric acid, found by us for different alloys, are summarized in Table 2.

$$Ba_3Bi_{2\,cryst} + 6HCl_{soln} = 3BaCl_{2\,soln} + 2Bi_{cryst} + 3H_{2\,gas}.$$

On the basis of these data a value of -258.4 ± 1.8 kcal./gram-formula can be taken for the enthalpy of the reaction of Ba_3Bi_2 with dilute hydrochloric acid.

In combination with the known values for the enthalpies of formation and solution of hydrogen chloride and barium chloride [2] a value of 128.1 ± 1.8 kcal./gram-formula is obtained for the enthalpy of formation of barium bismuthide.

$$3Ba_{cryst} + 2Bi_{cryst} = Ba_3Bi_{2\,cryst} + 128.1 \pm 1.8 \text{ kcal.}$$

The value obtained by us differs from that found by Kubaschewski and Villa [6], who found the value of the enthalpy to be equal to -160 ± 10 kcal. by the method of directly determining the heat of mixing barium with

TABLE 1

Alloy no.	Enthalpy of reaction (1) (in kcal/gram-formula
1	—159.8
2	—160.2
3	—160.8

TABLE 2

Alloy no.	Enthalpy of reaction (2) (in kcal/gram-formula)
1	—257.6. —257.5
2	—260.2. —260.4
3	—258.3. —258.3

bismuth. If anything the method used by us can give somewhat high absolute values, which means that the value of -160 kcal. for the enthalpy of formation of barium bismuthide is definitely in error. The possible reason for Kubaschewski and Villa obtaining a higher (in absolute value) value for the enthalpy of formation of the barium compound is indicated above.

In completely the same manner the enthalpy of formation of the alloy having the composition BaBi was found to be equal to -40.2 ± 1.4 kcal./gram-formula (the system Ba–Bi was studied only in the interval 0–30 at. % barium [7], but by analogy with the system Sr–Bi, studied in greater detail [8], it can be assumed that such a compound, BaBi, does exist).

A comparison of the course of the enthalpies of formation of compounds of magnesium with the elements of the main subgroup of Group V with the course of the enthalpies of formation of the compounds of these elements with barium is not without interest, although the information on the latter is still incomplete. This comparison is shown in the Figure, from which it can be seen that if the transition from Mg_3N_2 to Mg_3Bi_2 is characterized by a nearly 3-fold reduction in the heat of formation [9], then the transition from Ba_3N_2 [2] to Ba_3Bi_2 is accompanied by a considerable increase in the heat of formation.

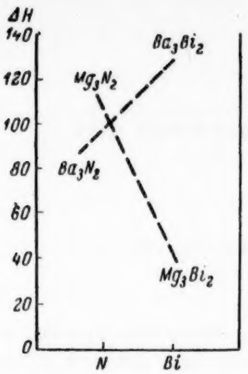
We determined the density of Ba_3Bi_2, proving to be equal to 6.12 g/cm^3 (at 20°). The density of Mg_3Bi_2 is 5.84 g/cm^3 (at the same temperature).

A substantial increase in the heat of formation in the transition from magnesium bismuthide to barium bismuthide is also accompanied by changes in the volume ratios existing in the systems Mg–Bi and Ba–Bi. The formation of Mg_3Bi_2 from the elements is accompanied by a slight increase in the volume (0.6 ml/gram-formula), whereas in the formation of Ba_3Bi_2 the volume is reduced by 17.2 ml/gram-formula.

In the system Mg–Bi–N_2, even at comparatively low nitrogen pressures, the stable forms are Mg_3N_2 and Bi, whereas in the system Ba–Bi–N_2, at all actually realized nitrogen pressures, the stable forms are Ba_3Bi_2 and N_2.

The nitrides of magnesium and barium represent saltlike compounds, and a reduction in the heat of formation in the transition from Mg_3N_2 to Ba_3N_2 is probably explained by the substantial increase in the ionic radius in going from Mg^{+2} to Ba^{+2}; the reduction in the energy of the lattice, associated with this, is apparently not compensated by a reduction in the energy of ionization, occurring in the direction from Mg to Ba.

The bismuthides of both metals are quite typical intermetallic compounds, and consequently a change in the heat of formation, accompanying the replacement of magnesium by barium, naturally obeys a different law. This difference in the course of the enthalpies of formation of the magnides and barides of the elements of the main subgroup of Group V points without equivocation to the primitive nature of the whole series of attempts made to generalize the rules for the enthalpies of formation of binary compounds, in particular, to the primitive nature of the conception of electronegativity as being a constant specific value, characterizing the elements [10, 11]. From the viewpoint of this conception, as is known, the replacement by barium should result in an increase in the heats of formation of both the nitride and the bismuthide, which is contradictory to experimental data.



Course of the enthalpies of formation of compounds of barium and magnesium with nitrogen and bismuth.

SUMMARY

1. The enthalpy of formation of lithium bismuthide, Li_3Bi, was found to be equal to -39.5 ± 0.5 kcal./gram-formula.

2. The enthalpies of formation of Ba_3Bi_2 and BaBi were respectively found to be equal to -128.1 ± 1.8 and -40.2 ± 1.4 kcal./gram-formula.

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THE ENTHALPY OF FORMATION OF LITHIUM, MAGNESIUM AND ZINC ARSENIDES

S. M. Ariya, M. P. Morozova, Khuan Tszi-tao and E. Volf

Recently [1] a new value, 18.0 kcal./mole, was published for the enthalpy of formation of arsine, differing considerably from the value that had been generally accepted up to now 43.6 kcal./mole) [2].

A more accurate determination of the value of the enthalpy of formation of arsine makes it possible to determine the enthalpies of formation of the arsenides of lithium, magnesium and zinc on the basis of the values of the enthalpies of their reaction with dilute hydrochloric acid, proceeding with the formation of arsine.

The enthalpy of the process for the reaction of magnesium arsenide with hydrochloric acid was determined by S. A. Shchukarev, S. M. Ariya and G. A. Lakhtin [3], and then by us. It is −215.3 kcal./gram-formula:

$$Mg_3As_{2\,cryst} + 6HCl_{soln} = 3MgCl_{2\,soln} + 2AsH_{3\,gas} + 215.3 \text{ kcal.}$$

On the basis of the old value for the enthalpy of formation of arsine a hypothetical value of −46±3 kcal./gram-formula was assumed in the cited paper for the enthalpy of formation of magnesium arsenide. When the new value for the enthalpy of formation of arsine is used the enthalpy of formation of magnesium arsenide proves to be equal to −96±3 kcal./gram-formula:

$$3Mg_{cryst} + 2As_{cryst} = Mg_3As_{2\,cryst} + 96 \pm 3 \text{ kcal.}$$

It is timely to mention that the enthalpy of formation of magnesium arsenide (−46 kcal./gram-formula) obtained on the basis of the old value for the enthalpy of formation of arsine contradicts the stability of this compound. In combination with the indicated value, the huge increase in the entropy, which should accompany the decomposition of magnesium arsenide (not less than 110 electron-volts), would assure a low thermal stability for Mg_3As_2 (the substance should suffer decomposition when heated in a stream of an inert gas even at 600-700°, which is not observed in practice).

$$Mg_3As_{2\,cryst} = 3Mg_{gas} + \tfrac{1}{2}As_{4\,gas}.$$

The enthalpy for the reaction of zinc arsenide with hydrochloric acid was determined to be equal to −44.5 kcal./gram-formula [4].

Taking the enthalpy of formation of arsine as equal to 44.2 kcal./mole, the Italian authors found the heat of formation of zinc arsenide to be equal to 30.3 kcal./gram-formula. However, they admitted an error into their calculations; actually, the found value for the enthalpy of the reaction of zinc arsenide with hydrochloric acid, in combination with the old value for the enthalpy of formation of arsine, leads to a negative heat of formation for the arsenide, and specifically, −30.3 kcal./gram-formula.

However, the endothermic nature of zinc arsenide contradicts the chemistry of this compound, easily obtained by the reaction of the elements and not showing any signs of decomposition when heated in vacuo at 600°.

We repeated the determination of the enthalpy for the reaction of zinc arsenide with hydrochloric acid. The enthalpy of this process proved to be equal to −53.5 kcal./gram-formula:

$$Zn_3As_{2\,cryst} + 6HCl_{soln} = 3ZnCl_{2\,soln} + 2AsH_{3\,gas} + 53.5 \text{ kcal.}$$

The considerable divergence with the data of [4] can probably be explained by the fact that these authors did not have the present type of calorimeter, and instead used a simple Dewar vessel for the calorimetric determinations.

The value for the enthalpy that we obtained by the above indicated reaction, coupled with the new value for the enthalpy of formation of arsine, leads to a value of −30.5 kcal./gram-formula for the enthalpy of formation of Zn_3As_2:

$$3Zn_{cryst} + 2As_{cryst} = Zn_3As_{2\,cryst} + 30.5 \pm 3 \text{ kcal.}$$

Assuming the old value for the enthalpy of formation of arsine (43.6 kcal./mole), instead of the above value we would have obtained +20.5 kcal., which, as has already been indicated above, is in complete disagreement with the properties of zinc arsenide. As a result, this circumstance clearly indicates the erroneous nature of the old value for the enthalpy of formation of arsine, figuring up to now in all of the reviews on thermochemistry [2, 5].

A study of lithium arsenide, Li_3As, also leads to a similar result. We found the enthalpy for the reaction of lithium arsenide with dilute hydrochloric acid to be equal to −101.8 kcal./gram-formula:

$$Li_3As_{cryst} + 3HCl_{soln} = 3LiCl_{soln} + AsH3_{gas} + 101.8 \text{ kcal.}$$

This value, coupled with the old value for the enthalpy of formation of arsine, leads to a value of −56.3 kcal./gram-formula for the enthalpy of formation of lithium arsenide.

Earlier [6] we had determined the value for the enthalpy of formation of lithium stibnide, Li_3Sb. It proved to be equal to −77 kcal./gram-formula. In other words, if the old value for the enthalpy of formation of arsine is taken, then the impression is created that lithium stibnide is a much more exothermic compound than the arsenide. Together with this, Lebeau [7] noted that arsenic displaces antimony from its compound with lithium. This fact, confirmed by us, is incompatible with the just indicated relationship of the enthalpies of formation of Li_3As and Li_3Sb.

In combination with the new value for the enthalpy of formation of arsine, the value obtained by us for the enthalpy of the reaction of lithium arsénide with dilute hydrochloric acid leads to a greater absolute value for the enthalpy of formation of lithium arsenide than for the case of Li_3Sb, and specifically −81.3 kcal./gram-formula:

$$3Li_{cryst} + As_{cryst} = Li_3As_{cryst} + 81.3 \text{ kcal.}$$

In other words, Li_3As proves to be a somewhat more exothermic compound than Li_3Sb, which is in agreement with the fact that antimony is displaced by arsenic from its compound with lithium.

SUMMARY

1. The enthalpies of formation of the arsenides of lithium, magnesium and zinc were determined, respectively being equal to −81.3± 2, −96± 3 and −30.5± 3 kcal./gram-formula.

2. A number of facts were mentioned, indicating that the recently proposed value for the enthalpy of formation of arsine is in agreement with the data on the thermal stability of the arsenides studied in this paper.

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ANODES FROM URANIUM DIOXIDE IN A MOLTEN CHLORIDE ELECTROLYTE

M. V. Smirnov and L. E. Ivanovsky

Studies devoted to electrochemical investigations of electrodes composed from semiconductors in molten salt electrolytes are absent in the literature. Many semiconductors belong to the class of metal oxides, the conductivity of which varies within very wide limits. The poorest conductors of all are the metal oxides of normal valence, such as BeO, ThO_2, TiO_2, Nb_2O_5, Ta_2O_5, UO_3 [1, 2]. In the transition to the lower oxides of these metals the conductivity increases so sharply [3, 4] that electrodes can be prepared from them, and they can be used in electrolysis.

We studied the behavior of the anodes from uranium dioxide in molten alkali metal chlorides. Based on the literature data [5], its conductance at 478-992° varies in the limits 0.247-1.282 $ohm^{-1} cm^{-1}$; it strongly depends on the degree of condensation of the particles, the purity and the composition of the dioxide.

Electrolysis in a Molten Chloride Bath With a Uranium Dioxide Anode

The starting dioxide was prepared by the reduction of uranium oxide (U_3O_8) with hydrogen at 700°. The dioxide had a black color. Chemical analysis revealed that its composition corresponded to the empirical formula $UO_{2.04}$. The dioxide powder was moistened with a solution of paraffin in benzene. About 0.01 g of paraffin was taken per gram of dioxide, which served as a binding material. Under a pressure of about 3000 kg/cm^2 the electrodes were pressed into a cylindrical shape (diameter 8 mm, length 15 mm), which were then sintered, being heated for 4 hours at 1350° in a vacuum of the order of 10^{-3} mm. The sintered electrodes showed sufficient mechanical strength. The conductance showed considerable increase after sintering and the color of the electrodes changed (they became dark-brown). Analysis for carbon gave negative results.

The electrolysis experiments were run in a closed apparatus, the construction of which is schematically shown in Fig. 1. It represented a quartz test tube, hermetically sealed on top. The cathode, a molybdenum wire, was contained in the quartz test tube through an opening, which was tightly covered with an asbestos diaphragm. In order to eliminate the liberation of the alkali metal, exerting a strong decomposition action on quartz glass, lead chloride was added to the test tube. The amount of electricity passed was determined from the amount of metal that separated at the cathode during electrolysis. In the anode area the starting electrolyte was a molten eutectic mixture composed of lithium and potassium chlorides. The uranium dioxide anode was turned in a lathe in such a manner that it could be fitted in the opening present in the quartz tube. The lower portion of the anode was immersed in the electrolyte, while its upper portion in the test tube was clamped to a platinum rod, which served as the conductor of the current above the electrolyte level. The electrolysis was run at 650° in an atmosphere of pure argon. The current strength was maintained constant during the whole experiment. On conclusion of electrolysis the electrolyte was analyzed for its content of tetra- and hexavalent uranium.

In the Table we give the results of three experiments, run with different anodic current densities.

In all of the experiments the analyses revealed that only hexavalent uranium is contained in the electrolyte. The melt had a color of strong tea, while the cold electrolyte was colored a yellow-green, whereas the melts containing tetravalent uranium are colored a dark-green, and the cold salts an emerald-green.

As can be seen from the date in the Table, the yield on the current of UO_2^{++} ions in the electrolyte is equal to 100% (the somewhat lower yield in the first experiment is apparently due to error in the analysis). During the electrolysis the evolution of gases was observed at the anodes, but their surface gradually become covered with

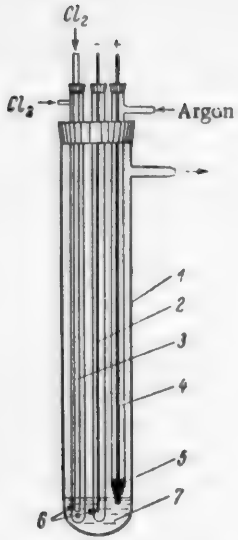

Fig. 1. Schematic drawing of electrolysis cell. 1) Quartz test tube, 2) molybdenum cathode, 3) chlorine electrode, 4) platinum conductor, 5) asbestos diaphragm, 6) anode from uranium dioxide, 7) electrolyte.

a dense crystalline crust having a blue-black color, which sharply differed from the color of the electrode mass (dark-brown).

The experimental results show that during electrolysis the uranium dioxide anodes dissolve due to the transition of UO_2^{++} ions into the melt. Since the starting oxide did not correspond to an exact stoichiometric composition of the dioxide, but contained some excess of oxygen, with duration of electrolysis the anode should gradually become enriched in oxygen.

It is known [6] that uranium forms with oxygen a one-phase system of continuous composition ranging from UO_2 to $UO_{2.33}$. The excess oxygen of these oxides occupies an intermediate position in the UO_2 lattice (of the fluorspar type) and can be freely transposed in it [7]. In measure with transition of the UO_2^{++} ions into the electrolyte the oxygen, apparently, diffuses into the depth of the oxide phase. When the limiting composition, corresponding to $UO_{2.33}$, is achieved in the surface layer of the anode, then the second phase of uranium oxide (U_3O_8) should appear. It was actually observed in our experiments as a black crust on the surface of the anodes.

$$UO_{2.04} \xrightarrow{-UO_2^{++}} UO_{2.33} \xrightarrow{-UO_2^{++}} U_3O_8$$

That uranyl ions are actually formed in the electrolyte during the solution of anodes composed of uranium oxides of variable composition was confirmed by a special experiment, in which after the accumulation of uranium in the anolyte further electrolysis was now run without a separation of the anode and cathode areas in the cell. A weakly held black crystalline precipitate separated on the molybdenum cathode, which, in contrast to metallic uranium, failed to dissolve in hydrochloric acid. The increase in weight, obtained when the precipitate was ignited in the air to uranium oxide, revealed that it was pure uranium dioxide.

The results of this experiment are of interest in a different respect. They support the possibility of oxy cations existing in molten chlorides [8]. It now becomes clear why it is uranium oxide, and not the metal, that frequently separates at the cathode when the electrolysis is run in open baths. Evidently, oxygen not only decomposes chloride melts, containing uranium tetrachloride, with the formation of the dioxide or of oxygen-containing salts, but also oxidized uranium to uranyl ions, which remain in the electrolyte and during the electrolysis of the former are discharged at the cathode, giving a precipitate of the dioxide.

Expt. nos.	Anodic current density (A/cm^2)	Amt. of electricity passed (A/hr)	Found U in electrolyte (g)	Yield on current of UO_2^{++} ions in electrolyte (in %)
1	0.01	0.090	0.386	96.5
2	0.10	0.196	0.870	100.0
3	1.00	0.250	1.110	100.0

It was also of interest to elucidate the manner in which uranium oxide anodes behave in the presence of a reducing agent, namely carbon monoxide. For this we ran a special experiment, in which the anode during the electrolysis was continuously washed with pure carbon monoxide. Analysis of the electrolyte after the experiment revealed that it contained about 10% of tetravalent uranium. However, the total amount of uranium, found in the electrolyte, corresponded to a 100% yield based on the current in the melt, in accord with the electrode reaction: $UO_2 - 2e \rightarrow UO_{2\,\text{molten}}^{++}$. Evidently, the tetravalent uranium was obtained as the result of

secondary reaction involving the reduction of the uranyl ions in the melt by carbon monoxide: $UO_2^{++}{}_{molten} + CO = U^{4+}{}_{molten} + CO_3^{--}{}_{molten}$, and not as the result of the primary electrode reaction: $UO_2 + 2CO - 4e = U^{4+}{}_{molten} + 2CO_2$.

Polarization of Uranium Dioxide Anodes During the Electrolysis of a Molten Chloride Bath

Qualtitative experiments reveal that uranyl ions are formed when uranium dioxide anodes are used in the electrolysis of a molten chloride electrolyte. However, these experiments cannot answer the question as to which electrode reaction is responsible for the dioxide going into solution: whether the ions migrate into the electrolyte directly from the dioxide lattice, similar to the anodic solution of metals, or whether the dioxide is chlorinated at the anode by the chlorine that is liberated as the result of the discharge of Cl^- ions. To answer this question we made a study of the anodic polarization of uranium dioxide electrodes.

The experiments were run in a closed quartz cell, the same as was used in the previous experiments (Fig. 1). The electrolyte was a eutectic mixture of lithium and potassium chlorides fused at 550°. The melt was first blown with dry hydrogen chloride to remove any possible traces of moisture (the anode was not immersed in the electrolyte during this period). To remove the gases the cell was evacuated, and then was filled with pure argon. The readings were begun 10 minutes after the anode was immersed in the melt. The anode potentials were measured after a 4-5 second polarization at the moment of turning off the polarizing current, using a recording oscillograph, relative to the chlorine electrode. The construction of the chlorine electrode had been described earlier [9]. It was placed in a separate quartz test tube with a diaphragm, which prevented the chlorine from dropping on the anode. The current density was calculated on the basis of the geometric surface of the anode immersed in the electrolyte. It was varied in wide limits ranging from 0.001 to 1 A/cm^2.

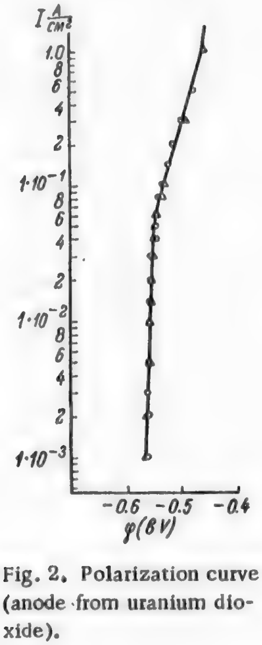

Fig. 2. Polarization curve (anode from uranium dioxide).

The measurement results (relative to the chlorine electrode) are shown in Fig. 2. They show that at small current densities (below 0.05 A/cm^2) the anodic process proceeds with insignificant polarization (the anodic polarization increases by 0.013 V, while the current density is increased approximately 100-fold). The anode potential is approximately 0.57 V more negative than the potential of the chlorine electrode, which corresponds to a chlorine pressure over it of the order of 10^{-5} atm. When the current density reaches a value of 0.06 A/cm^2, the anodic potential begins to increase much more rapidly with the current density. This break in the polarization curve, as was shown experimentally, is not associated with a change in the nature of the ions, migrating into the electrolyte during the solution of the anode. In the whole interval of current densities studied the anodic yield of UO_2^{++} ions, based on the current, is practically equal to 100%.

The anodic solution of uranium dioxide, similar to the metals, proceeds with slight polarization, apparently associated with concentration changes in the pre-electrode layer of the electrolyte, at a potential close to the equilibrium potential. The electrode reaction represents direct migration of the UO_2^{++} ions into the melt without the intermediate discharge of chlorine ions. The potential of the electrode should be determined by the molar concentration of UO_2^{++} ions in the electrolyte. If such is the case, then by measuring the temperature dependence of the e.m.f. of the galvanic element: UO_2 UO_2Cl_2 (melt) Cl_2, C, we can find the value of the thermodynamic parameters of uranyl chloride, for which there fail to be any literature data at the present time [10].

The break in the polarization curve is probably conditioned by the formation of a second oxide phase (U_3O_8) in the surface layer of the anode, in which the diffusion of oxygen is more difficult than for the case of its diffusion in the oxide phase of variable composition ($UO_{2.00}$-$UO_{2.33}$).

Since the potential for the discharge of UO_2^{++} ions at the cathode is more positive by approximately 1 V than the potential for the liberation of metallic uranium, then even slight contaminations of the electrolyte by oxygen should lead to contamination of the cathodic deposits of the metal by the dioxide.

SUMMARY

1. Electrodes were prepared from uranium dioxide, which could be used as anodes in the electrolysis of molten chlorides at current densities up to 3 A/cm^2.

2. The behavior of uranium dioxide anodes of composition $UO_{2.04}$ in a molten mixture of potassium and lithium chlorides was studied at 650°. It was established that they go into solution in the interval of current densities ranging from 0.001 to 1 A/cm^2, forming uranyl ions in the electrolyte in 100% yield based on the current. The excess oxygen accumulates in the anode, while the UO_2^{++} ions, in their discharge at the cathode, give a deposit of uranium dioxide of stoichiometric composition.

3. The polarization of uranium dioxide anodes of composition $UO_{2.04}$ was measured at 550° in a melt of chlorides. It was found that at current densities below 0.05 A/cm^2 the potential at the anode is more negative by 0.57 V than the potential of the chlorine electrode, and changes but slightly with the current density. More substantial polarization is observed above 0.05 A/cm^2. It is postulated that electrodes made from uranium dioxide behave in melts the same as do metallic electrodes. Their potential is determined by the molar concentration of UO_2^{++} ions in the electrolyte.

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SOME PHYSICOCHEMICAL PROPERTIES OF BARIUM, COBALT AND COPPER CIS-BOROTUNGSTATES

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Literature data, relating to a study of the physiocochemical properties of borotungstates (in the future we will designate them as b. t.), are meager. Thus, A. V. Rakovsky and A. V. Babaeva [1] studied the dissociation pressure of the crystallohydrates of pentasubstituted barium b. t. $Ba_5H_8[B(W_2O_7)_6]_2 \cdot xH_2O$ under isothermal conditions by the van Bemnelen method and established the existence of hydrate forms with 54.77–52.32, 39.16 and 36.19 moles of H_2O, calculated on the basis of total oxides $BaO \cdot B_2O_3 \cdot 24WO_3$.

In the literature [2] cobalt b. t. $Co_5H_8[B(W_2O_7)_6]_2 \cdot x\,H_2O$ is described as a pentasubstituted salt, crystallizing with 18 moles of H_2O. The salt forms current-red solutions with a high specific gravity; thus, a solution not saturated at 19° has d 3.36-3.37. Kahlbaum [3] determined the solubility of cobalt b. t. in water in the temperature interval 16.2–21.8° without indicating the composition of the solid phases. The parts of salt found in 100 parts of water were: at 16.2°–306.8, at 18.5°–288, at 19.6°–299.7, and at 21.8°–286.

Copper b. t. $Cu_5H_8[B(W_2O_7)_6]_2 \cdot xH_2O$, described by Klein [2], separates from solutions as prismatic crystals, readily soluble in water; a solution saturated at 20° contains 80% salt and has d 2.6; with elevation of the temperature the solubility of the salt apparently increases slightly. At 165° the salt loses about 14 moles of H_2O and becomes white. Copaux [4] obtained a pentasubstituted copper b. t. Kahlbaum [3] described a crystallohydrate of the disubstituted copper salt, separating from solutions as tablet crystals. The author indicates that during crystallization a nearly white salt separated in the first fraction, with sky-blue crystals appearing later. The solubility of the salt in water was determined without studying the composition of the solid phase. The parts of salt found in 100 parts of water at 20.8° was 363.7, and at 20.9° it was 360.3. The specific gravity of the copper b. t. solution, saturated at 15.5°, was 3.0073.

EXPERIMENTAL

Synthesis of Cobalt and Copper Borotungstates. The starting compound for the preparation of cobalt and copper b. t. was the barium salt, for which the method of preparation had been developed by us earlier [5].

The cobalt salt of b. t. acid was obtained by adding an approximately 10% cobalt sulfate solution to a 6% barium b. t. solution until all of the barium had precipitated, but without an excess of $CoSO_4$. After standing for 16-18 hours the cobalt b. t. solution was carefully filtered and evaporated on the water bath to separate the crystals of the compound. Analysis of the obtained salt gave the following results: H_2O–9.74%, CoO–6.41% (for the salt without hydration water); calculated amount of CoO–6.28%. The formula $Co_5H_8[B(W_2O_7)_6]_2 \cdot 32H_2O$ corresponds to the found composition.

The copper salt of b. t. acid was obtained in the same manner as the cobalt salt from barium b. t. and copper sulfate.

Analysis of the obtained salt gave the following results: H_2O–10.83%, CuO–6.62%; calculated (for the salt without hydration water) CuO–6.52%. On the basis of the analysis results the obtained salt should be assigned the formula $Cu_5H_8[B(W_2O_7)_6]_2 \cdot 36H_2O$.

The studies were made by us in the temperature interval from 1 to 80° in a thermostat of the usual construction; the variations in the temperatures did not exceed ± 0.1°.

The solid phase was separated in the following manner: the solution, remaining in the vessel after analysis of the liquid phase had been completed, was suction-filtered as completely as possible through a Buchner funnel using a water-jet pump; the crystals were dried with filter paper in the test tube and also after their extraction from it. Samples of the liquid and solid phase were weighed in platinum crucibles. In analyzing the liquid phase the solution was first carefully evaporated to dryness on an air bath using a weak flame, after which the crucible was kept on the air bath at a temperature of about 300° for 30 minutes, and then it was ignited for 2-3 minutes over the free flame. The residue was a mixture of the oxides $5BaO \cdot B_2O_3 \cdot 24WO_3$. In analyzing the solid phase 1-2 ml of water was added to the weighed sample of crystals, and then the procedure was the same as described above. The water was added for the reason that at times the salt crystals failed to dehydrate uniformly, with the result that the substance spattered and was ejected from the crucible; when the solution is evaporated the substance forms a thin layer on the surface of the crucible and the dehydration proceeds both uniformly and smoothly.

On the basis of the obtained data we calculated the content of the salt $Ba_5H_8[B(W_2O_7)_6]_2$ in the liquid and solid phases, and also the composition of the crystallohydrate.

TABLE 1

Solubility of Barium Borotungstate

Temperature	Amount of $Ba_5H_8[B(W_2O_7)_6]_2$ in liquid phase (in %)	Compo. of solid phase (%)		No. H_2O molec. in compo. of the crystallohydrate
		$Ba_5H_8[B(W_2O_7)_6]_2$	H_2O	
1°	11.96	85.13	14.87	53.48
20	48.84	85.78	14.22	51.14
40	65.56	86.06	13.94	50.14
60	71.61	87.88	12.12	43.59
80	74.66	89.33	10.67	38.38

a) Solubility of the Barium Salt. The starting substance $Ba_5H_8[B(W_2O_7)_6]_2 \cdot 46H_2O$ was prepared by the earlier developed method.

The results of studying the solubility are presented in Table 1. Analysis of the solid phases indicates a jumplike change in the water content at temperatures above 40°; apparently, a portion of the water in barium b. t. forms solid solutions, while another portion represents ordinary water of crystallization.

The obtained data testify to the fact that barium b. t. is readily soluble in water; the temperature coefficient of the solubility is substantial, and the increase in solubility is especially sharp in the temperature interval from 1 to 40°; in the temperature region from 50° and higher the rise in solubility is less intense.

Some of the hydrate forms obtained by us, and specifically the hydrates with 53.48 and 38.38 moles of H_2O, have been described earlier [1] as being solid solutions; we were the first to obtain the hydrate forms with 51.14, 50.14 and 43.59 moles of H_2O.

b) Solubility of the Cobalt Salt. To study the solubility we used the salt of composition $Co_5H_8[B(W_2O_7)_6]_2 \cdot 32H_2O$. The method used to study the solubility was similar to the one just described for the barium salt.

The results of studying the solubility are presented in Table 2.

The solubility of cobalt b. t. increases smoothly in measure with temperature increase; apparently, a portion of the hydration water forms solid solutions; cobalt b. t. is readily soluble in water; the solubility temperature coefficient of the cobalt salt is smaller than that of the barium salt. All of the hydrate forms of the salt that we obtained were previously unknown in the literature.

TABLE 2

Solubility of Cobalt Borotungstate

Temperature	Amount of $Co_5H_8[B(W_2O_7)_6]_2$ in liquid phase (in %)	Compo. of solid phase (%)		No. H_2O molec. in compo. of the crystallohydrate
		$Co_5H_8[B(W_2O_7)_6]_2$	H_2O	
1°	58.60	84.72	15.28	60.90
20	67.36	85.10	14.90	59.16
40	72.74	86.03	13.97	54.87
60	76.59	87.76	12.24	47.13
80	78.86	88.45	1.55	44.12

Thermographic Study of Barium and Cobalt Borotungstates*

An N. S. Kurnakov pyrometer, with both direct and differential recording, was used to study the heating curves of barium and cobalt b. t; the recording was made in the temperature interval from 18 to 250°. The duration of heating was 40 minutes.

The obtained data are shown in Figs. 1 and 2. Curve 1 on these plots corresponds to the heating of the sample, and Curve 2 corresponds to the differential recording, showing the presence of a difference in the temperature of the sample and the standard during the heating process.

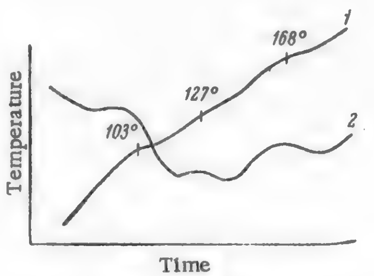

Fig. 1. Thermogram of barium borotungstate.
Explanation in text.

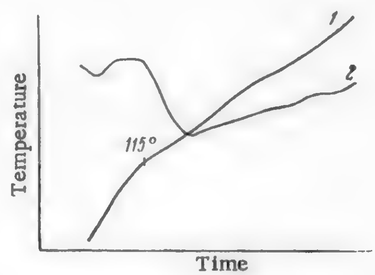

Fig. 2. Thermogram of cobalt borotungstate.
Explanation in text.

a) Barium Borotungstate. For the study we took the salt of composition $Ba_5H_8[W_2O_7]_6]_2 \cdot 46H_2O$. The obtained thermogram (Fig. 1) indicates the existence of three endothermic effects at 103, 127 and 168°. By gravimetric analysis it was established that at 103° the salt loses 14 moles of water; consequently, at this temperature the solid phase contains 32 moles of H_2O; at 127° 26 moles of water are lost, and at this temperature the solid phase contains 20 moles of water; at 168° the salt loses 43 moles of water; the solid phase at this temperature contains 3 moles of water; the last 3 moles of hydration water are removed at above 250°. As a result, the new hydrates of barium b. t. with 32, 20 and 3 moles of water were disclosed by the thermographic method.

b) Cobalt Borotungstate. For study we took the salt of composition $Co_5H_8[B(W_2O_7)_6]_2 \cdot 32H_2O$. The obtained thermogram (Fig. 2) indicates the existence of one endothermic effect at 115°; at this temperature the salt loses 29 moles of water and the hydrate of composition $Co_5H_8[B(W_2O_7)_6]_2 \cdot 3H_2O$ is formed. The last 3 moles of hydration water are lost above 115°, without any heat effect; then the salt-forming water is lost, and the heteropoly compound begins to decompose. Thermographic study reveals that 3 moles of the hydration water in the salts are bound more firmly than are the remainder; however, the stability of the bond of the salt-forming water is substantially greater and its loss, observed above 250°, is associated with decomposition of the heteropoly anion.

* E. V. Buris participated in this portion of the work.

Spectrophotometric Study of Solutions of Copper and Cobalt Borotungstates

A Hilger spectrophotometer was used for the study. The obtained data are shown in Figs. 3 and 4; 1% solutions of the salts were used in the study.

The performed investigation made it possible to establish that a broad absorption region with a maximum in the green portion of the spectrum is characteristic for the cobalt b. t. solution; for copper b. t. a sharp rise in

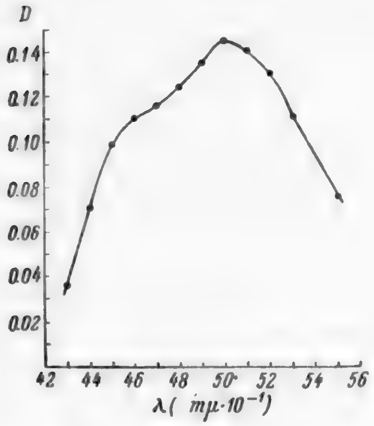

Fig. 3. Curve for the light absorption of cobalt borotungstate solution.

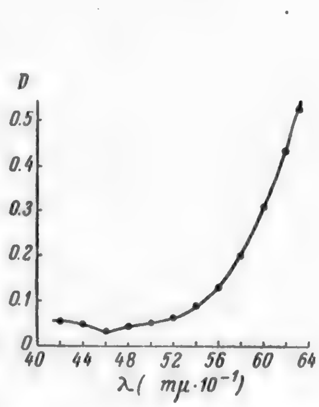

Fig. 4. Curve for the light absorption of copper borotungstate solution.

absorption was observed in the transition from the green portion of the spectrum to the region of longer wavelengths. The character of the light absorption depends primarily on the properties of the salt cations; the influence of the heteropoly anion is expressed more weakly.

SUMMARY

1. Cobalt and copper borotungstates were obtained by the exchange decomposition of barium borotungstates with cobalt and copper sulfates.

2. The solubility of barium and colbalt borotungstates was studied in the temperature interval from 1 to 80°.

3. The existence of hydrates of barium borotungstate with 51.14, 50.14, 43.59 and 38.38 moles of H_2O was established by the solubility method. Hydrates with 60.9, 59.15, 54.87, 47.13 and 44.12 moles of H_2O were obtained for cobalt borotungstate.

4. The existence of the hydrates of barium borotungstates with 32.20 and 3 moles of H_2O and of the hydrate of cobalt borotungstate with 3 moles of H_2O was established by the thermographic method.

5. A spectrophotometric study was made of solutions of cobalt and copper borotungstates. A maximum was established on the absorption curve of the cobalt salt; it was shown that the character of the light absorption depends mainly on the properties of the salt cations.

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* Original Russian pagination. See C. B. Translation.

HETEROTRIACIDS

VI. SOME PROPERTIES OF HETEROTRIACIDS

A. I. Kokorin and N. A. Polotebnova

In previous communication [1-3] we described the synthesis of a number of heterotriacids and established their composition. In particular, we studied the heterotriacids of phosphorus and silicon with a variable composition of the addenda, containing molybdenum and tungsten.

In the present communication we present the experimental data obtained by us in studying some of the more important properties of all of the heterotriacids synthesized by us earlier.

Some Physical Properties. All of the heterotriacids of phosphorus and silicon synthesized by us are crystalline substances. The crystals have the shape of regular octahedrons, frequently with cut edges.

The compounds, having molybdenum and tungsten as addenda,range in color from weak to intensely yellow, depending on the amount of molybdenum present in the composition of the polyanion. The tungstovanadium heterotriacids are colored orange-red, and the molybdovanadium compounds range in color from red-orange to ruby-red.

The amount of water of crystallization strongly depends on the crystallization conditions. The same heteropolyacid can crystallize with a different number of water molecules. The minimum amount of water, 15-16 molecules, was revealed in the crystallohydrates of phosphomolybdovanadic and phosphomolybdotungstic (I) acids, and the maximum, 37-38 molecules, in some samples of the phosphotungstovanadic and silicotungstovanadic acids. Compounds with 24 and 28 molecules of water are obtained more frequently than the others. All of the crystallohydrates effloresce to a greater or less degree in the air, gradually changing to a powder. Here some of the heterotriacids begin to decompose with the separation of difficulty-soluble oxides of tungsten, molybdenum, vanadium and silicon. Of the heterotriacids the phosphomolybdovanadic acid is extremely stable, which does not decompose when stored in a closed flask for a number of years. It is more stable than the phosphomolybdic acid. The silico- and germani-molybdovanadic acids decompose more readily than the others. The phospho-, germani- and silicotungstovanadic heterotriacids are considerably more stable. The last belongs to the class of quite stable heterotriacids—its storage in a closed flask for more than two years failed to produce any changes. The phosphomolybdotungstic acids are not characterized by a great stability, while the analogous triacids with a central silicon atom show average stability. The storage of the latter for several months fails to result in any noticeable changes.

The gradual heating of the heterotriacids results in the stepwise removal of water. The water of the separate acids is held with variable strength. This problem is discussed in detail in a special study [4].

The synthesized compounds are quite stable in water solutions. However, on prolonged standing the color of the solutions fades, whichsuggests slow hydrolysis, and finally the solutions begin to turn cloudy. The time when cloudiness appears is a function of the nature of the inner sphere. Thus, the solutions of the phosphomolybdotungstic acids cannot stand long storage. The turbidity begins to appear within two to three weeks of storage, whereas in the case of the silicotungstovanadic acid solution the turbidity failed to appear even after two years of storage.

All of the heteropolyacids are readily soluble in the alcohols: ethyl, butyl, isobutyl, glycerol and cyclohexanol; in formaldehyde, benzaldehyde, acetone and cyclohexanone; in formic and glacial acetic acids.

TABLE 1

Melting Points of the Crystallohydrates of the Heteropolyacids of Phosphorus and Silicon

Heteropolyacid	Melting point (avg. of three determin.)
$H_7[P(Mo_2O_7)_5V_2O_6] \cdot 26H_2O$	47.5°
$H_7[P(W_2O_7)_5V_2O_6] \cdot 24H_2O$	52
$H_7[P(Mo_2O_7)_5W_2O_7] \cdot 26H_2O$	63
$H_7[P(Mo_2O_7)_4(W_2O_7)_2] \cdot 24H_2O$ . . .	70
$H_7[P(Mo_2O_7)_3(W_2O_7)_3] \cdot 24H_2O$ . .	78
$H_7[P(Mo_2O_7)_2(W_2O_7)_4] \cdot 22H_2O$ . .	89
$H_7[PMo_2O_7(W_2O_7)_5] \cdot 23H_2O$	88
$H_8[Si(Mo_2O_7)_5V_2O_6] \cdot 32H_2O$ . . .	39
$H_8[Si(W_2O_7)_5V_2O_6] \cdot 29H_2O$	39
$H_8[Si(Mo_2O_7)_5W_2O_7] \cdot 25H_2O$ . . .	37
$H_8[Si(Mo_2O_7)_4(W_2O_7)_2] \cdot 30H_2O$ . .	34
$H_8[Si(Mo_2O_7)_3(W_2O_7)_3] \cdot 31H_2O$ . .	34
$H_8[Si(Mo_2O_7)_2(W_2O_7)_4] \cdot 30H_2O$ . .	35
$H_8[SiMo_2O_7(W_2O_7)_5] \cdot 28H_2O$ . . .	37

In Table 1 we give the melting point data for a number of samples of heteroacids, obtained by us with a high and approximately close (within the separate groups of compounds) content of water of crystallization. The triacids with a central silicon atom show a very low melting point (34-39°), while the phosphomolybdotungstic heteropolyacids show a very high melting point (63-89°). The melting point of the crystallohydrates of the phosphomolybdotungstic acids is found to be directly related to the amount of tungsten in the heterotriacids when compared with molybdenum. With a constant amount of water of crystallization it increases with increase in the tungsten content. Numerous observations give basis to state that for the same compound the melting point strongly depends on the amount of water of crystallization. The greater the amount of water, the lower the melting point of the given compound.

Potentiometric Titration of Heterotriacids, Containing Vanadium. Physiocochemical investigations made to study the structure of heteropolyacids have been used for a comparatively long time and to a considerable degree have facilitated the development of theoretical representations as to their composition. Thus, for example, to determine the basicity of silicotungstic and silicomolybdic acids Copaux [5] used the method of measuring the conductivity of their solutions. Conductometric and potentiometric titration [6, 7] and a number of other methods can also be used for this purpose.

To elucidate the basicity of the heterotriacids and their stability toward alkalies we used the potentiometric titration method. An attempt to use the hydrogen and hydroxyantimony electrodes for this purpose did not lead to a positive result due to the partial reduction of the indicated electrode by a number of the compounds studied by us. The quinhydrone electrode could not be used in solutions showing alkaline. The glass electrode proved to be most suitable for our purposes. The use of potassium hydroxide solution instead of sodium hydroxide increases the possibility of titrating in a more alkaline medium.

To titrate the studied compounds we used a glass electrode with an LU-2 lamp amplifier and a potentiometer of the PPTV-1 type. The use of the indicated equipment makes it possible to determine the pH with an accuracy of ±0.02 units.

To eliminate the error of asymmetry of the glass electrode the apparatus was adjusted with the aid of buffer solutions, having pH 3, 7.09 and 9.11, which were prepared from mixtures of succinic or boric acid with the proper amounts of sodium tetraborate. The asymmetry potential of the glass electrode had the same value for all three of the indicated buffer solutions and remained stable with time.

In the present communication we give the potentiometric titration results for six heterotriacids with central atoms of phosphorus, silicon and germanium, containing vanadium in the composition of the addenda.

For titration we prepared 0.02M solutions of the heteroacids, proceeding from the weight of the total oxides, obtained after the complete removal of water at 460-480°. To 20 ml of the studied solution was added 20 ml of distilled water, and the titration was run with 0.2N potassium hydroxide solution. The temperature during titration was maintained constant at 18°. When the first titration jump was reached, then to establish the constancy of the potential it was necessary to boil, and then rapidly cool, after the addition of each portion of alkali. However, after this the potential was always measured at the same temperature of 18°. A correction was introduced for the values of the hydrogen ion concentration obtained by direct titration, which compensated for the change in the initial volume of the titrated solution during titration.

The study results are shown in Figs. 1 and 2.

Measurement of the Conductivity of Solutions of Heterotriacids, Containing Vanadium, and Their Potassium Salts. The conductivity measurements were made the same as had been described earlier [3]. The molar (μ) and equivalent (λ) conductance with dilution up to 1024 liters are given in Table 2. Further dilution up to 8192 liters fails to change the conductivity values. The equivalent conductance was calculated from the amount of gram-equivalents of alkali, consumed for the neutralization of the salt-forming hydrogen ions.

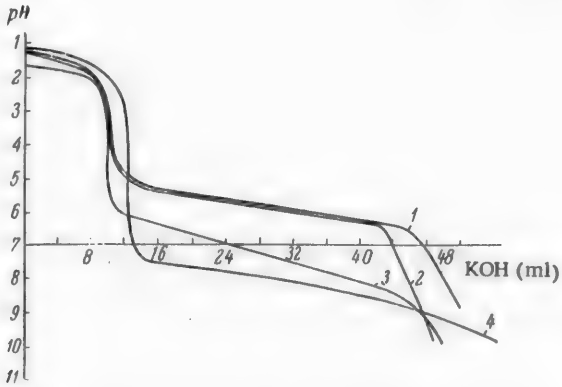

Fig. 1. Curves for the titration of phosphomolybdovanadic (1), germanimolybdovanadic (2), germanitungstovanadic (3) and phosphotungstovanadic (4) acids.

Measurement of the pH of Water Solutions of the Heterotriacids. Using a glass indicator electrode and a calomel semielement, the potentiometric method was used to measure the pH of the water solutions at three dilutions and a temperature of 25°.

For comparison with the experimentally found values, we calculated the theroetical pH of the same solutions, taking into consideration the hydrogen ion concentration and the activity coefficient. To find the latter we calculated the ionic strength of solutions J by the formula: $J = \frac{c_1 z_1^2 + c_2 z_2^2}{2}$, where c_1 is the hydrogen ion concentration, z_1 is the charge of the hydrogen ion, c_2 is the concentration of the heteropolyanion, and z_2 is the charge of the heteropolyanion. The values of the activity coefficients were taken from the data of [8].

The results of determing the pH are given in Table 3.

Some Chemical Properties of the Heterotriacids. A study of the heterotriacids revealed that all of these compounds precipitate under certain conditions the cations ammonium, rubidium, cesium, thallium, thorium, lead, zirconium and univalent mercury. These precipitates are either insoluble or difficultly soluble in mineral acids. In this respect the heterotriacids differ but slightly from the corresponding diacids.

Their behavior toward reducing agents and organic substances is of greatest interest.

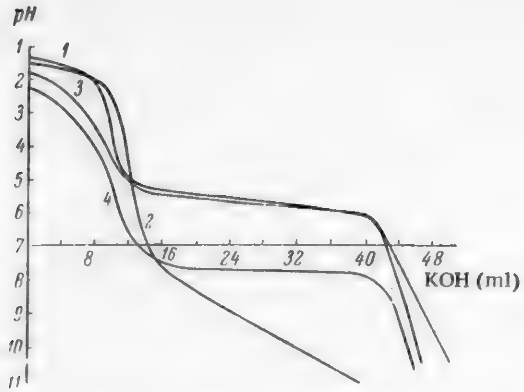

Fig. 2. Curves for the titration of silicomolybdovanadic (1), silicotungstovanadic (2), phosphomolybdic (3) and phosphotungstic (4) acids.

To study their behavior toward reducing agents we used 0.02M solutions of the heteropolyacids. As reducing agents we used 0.05N solutions of $FeSO_4$, $SbCl_3$, $SnCl_2$, and $TiCl_3$. The studies were made in both acid and alkaline media. The intensity of color and its stability was observed. All of the heterotriacids are reduced by strong reducing agents (Ti^{3+}, Sn^{2+}) to dark blue products. An increase in the tungsten content leads to the appearance of an increasing violet hue. The phospho-, silicomolybdovanadic and phosphomolybdotungstic I and II

TABLE 2

Molar and Equivalent Conductance of Solutions of Heterotriacids, Containing Vanadium, and Their Potassium Salts

Name of acid	Acid				Salt			
	μ_{256}	μ_{512}	μ_{1024}	λ_{1024}	μ_{256}	μ_{512}	μ_{1024}	λ_{1024}
Phosphomolybdovanadic	1546	1592	1705	341	537	580	630	126
Phosphotungstovanadic	1871	1959	2054	342	619	699	771	129
Silicomolybdovanadic	1532	1611	1722	344	527	615	722	144
Silicotungstovanadic	1876	1985	2083	347	577	650	742	124
Germaniumolybdovanadic	14[illegible]6	15[illegible]3	1705	341	554	625	725	145
Germanitungstovanadic	1504	1603	1665	333	530	587	612	124

acids are nicely reduced by antimony trichloride ($E_{Sb^{5+}/Sb^{3+}} = 0.64$ V). Consequently, their oxidation-reduction potential is greater than 0.64 V. However, it is not higher than 0.77 V, since the reduction of the indicated heteroacids by a ferrous salt solution ($E_{Fe^{3+}/Fe^{2+}} = 0.77$ V) fails to give a blue-colored solution, and it only turns green. The blue reduction products show a variable stability. The reduction products of silicomolybdovanadic acid show the greatest stability to the atmosphere and with respect to acids. The analogous acid with a central phosphorus atom also gives a blue product that is stable to the air. However, reduction in a strongly acid medium (above 1N) leads to a less intense color due to partial decomposition of the heteropolyacid. The stability of the reduction products of the heteroacids, containing tungsten in the nature of addendum, is found to depend on the content of the latter: the greater the tungsten content, the less stable the reduction products.

To study the behavior toward organic substances we added 0.5 ml of a solution of the organic compound to 0.5 ml of a 0.02M solution of the heteroacid. The organic substances that we tested were a 5% aqueous

TABLE 3

pH of Water Solutions of Heteropolyacids at Different Dilutions

Heteropolyacid	Concentration of acid (M)	[H⁺]	Ionic strength	Activity coefficient	pH	
					calc.	found
Silicomolybdotungstic acid (V)	10^{-3}	$4 \cdot 10^{-3}$	10^{-2}	0.98	2.41	2.46
	10^{-4}	$4 \cdot 10^{-4}$	10^{-3}	1	3.40	3.44
	$3.3 \cdot 10^{-5}$	$132 \cdot 10^{-6}$	$3.3 \cdot 10^{-4}$	1	3.88	3.90
Phosphomolybdotungstic acid (III)	10^{-3}	$5 \cdot 10^{-3}$	$1.5 \cdot 10^{-2}$	0.96	2.32	2.38
	10^{-4}	$5 \cdot 10^{-4}$	$1.5 \cdot 10^{-3}$	1	3.30	3.34
	$3.3 \cdot 10^{-5}$	$165 \cdot 10^{-6}$	$4.9 \cdot 10^{-4}$	1	3.78	3.82
Phosphomolybdovanadic	10^{-3}	$5 \cdot 10^{-3}$	$1.5 \cdot 10^{-2}$	0.96	2.32	2.43
	10^{-4}	$5 \cdot 10^{-4}$	$1.5 \cdot 10^{-3}$	1	3.30	3.36
	$3.3 \cdot 10^{-5}$	$165 \cdot 10^{-6}$	$4.9 \cdot 10^{-4}$	1	3.78	3.80
Silicomolybdovanadic	10^{-3}	$5 \cdot 10^{-3}$	$1.5 \cdot 10^{-2}$	0.96	2.32	2.43
	10^{-4}	$5 \cdot 10^{-4}$	$1.5 \cdot 10^{-3}$	1	3.30	3.35
	$3.3 \cdot 10^{-5}$	$165 \cdot 10^{-6}$	$4.9 \cdot 10^{-4}$	1	3.78	3.80
Silicotungstovanadic	10^{-3}	$6 \cdot 10^{-3}$	$2.1 \cdot 10^{-2}$	0.94	2.24	2.24
	10^{-4}	$6 \cdot 10^{-4}$	$2.1 \cdot 10^{-3}$	1	3.22	3.28
	$3.3 \cdot 10^{-5}$	$198 \cdot 10^{-6}$	$7 \cdot 10^{-4}$	1	3.70	3.74
Phosphotungstovanadic	10^{-3}	$6 \cdot 10^{-3}$	$2.1 \cdot 10^{-2}$	0.94	2.24	2.31
	10^{-4}	$6 \cdot 10^{-4}$	$2.1 \cdot 10^{-3}$	1	3.22	3.28
	$3.3 \cdot 10^{-5}$	$198 \cdot 10^{-6}$	$7 \cdot 10^{-4}$	1	3.70	3.74

cupferron solution, a 5% solution of 8-hydroxyquinoline in 2N acetic acid, a 7% solution of pyrogallol in saturated sodium sulfite solution, a 0.01% solution of diphenylamine in concentrated sulfuric acid, a 10% aqueous thiourea solution, a 10% solution of diphenylcarbazide in alcohol, a 1% alcohol solution of dimethylglyoxime, a 0.5% solution of benzidine in 50% acetic acid, and a 20% aqueous solution of urotropine.

Cupferron is precipitated from hydrochloric acid solution by all of the indicated compounds with the formation of yellow to orange-brown precipitates. (The diacids under similar conditions do not give precipitates).

With 8-hydroxyquinoline all of the heteropolyacids give yellow to brown precipitates, difficultly soluble in mineral acids. (The diacids of silicon give white precipitates).

With dimethylglyoxime the triacids of phosphorus give yellow precipitates, while the diacids give white precipitates, soluble in nitric and hydrochloric acids (1 : 1). The heteroacids with a central silicon atom are precipitated incompletely. The obtained precipitates are readily soluble in hot water.

With pyridine and urotropine all of the heterotriacids give variable colored precipitates, soluble in hydrochloric acid (1 : 1).

With anisidine the precipitates are white, and insoluble in acids.

Benzidine precipitates the studied compounds with simultaneous coloration of the solution over the white precipitate (partial reduction of the heteroacid). The precipitates are soluble in concentrated mineral acids.

Pyrogallol, diphenylcarbazide, hydroquinone, diphenylamine and thiourea reduce the heterotriacids to variably colored products, the color ranging from green and violet to reddish-brown and blue.

DISCUSSION OF RESULTS

Potentiometric titration, measurement of the conductivity and measurement of the pH values of the water solutions give basis to make a number of conclusions.

Attention is attracted to the distinct nature of the first titration jump for the triacids containing vanadium, especially when tungsten is contained in the addendum. This titration jump corresponds to the full basicity of heteropolyacids. The second titration jump, corresponding to the complete decomposition of the heteropolyanion,

i.e. to the final formation of the simple salts of the acids, entering into the composition of the acido complex, is absent for the phospho- and silicotungstovanadic acids. Their acido complex is so stable with respect to alkalies that it is not completely decomposed even when boiled. The distinctness of the first and second titration jumps is found to depend on the stability of the acido complex toward alkalies. The first titration jump is "diffuse" if the heteropolyanion is unstable (Fig. 2). The second titration jump is completely absent with a very stable heteropolyanion (Fig. 2, Curve 2).

The number of salt-forming hydrogen ions, neutralized by the potassium hydroxide solution, is equal to five for the vanadium-containing heterotriacids with a central germanium atom (independent of whether the second addendum is molybdenum or tungsten), and also for the vanadic heterotriacids of phosphorus and silicon with molybdenum as the second addendum, and it is equal to six for the phospho- and silicotungstovanadic heterotriacids. These data are in agreement with the potentiometric titration results, and also with the measurements of the conductivity and pH of the water solutions at the higher dilutions. Some deviation is observed for the phosphotungstovanadic acid (slightly more than 6 equivalents of alkali are consumed for the titration), however measurements of the conductivity and pH value of its water solutions indicate the presence of six salt-forming hydrogen ions.

As a result, compounds of theis type correspnd to the formulas: $H_5H_2[P(Mo_2O_7)_5V_2O_6]$, $H_5H_3[Si(Mo_2O_7)_5V_2O_6]$, $H_5H_3[Ge(Mo_2O_7)_5V_2O_6]$, $H_5H_3[Ge(W_2O_7)_5V_2O_6]$, $H_6H[P(W_2O_7)_5V_2O_6]$, $H_6H_2[Si(W_2O_7)_5 V_2O_6]$, where the hydrogen ions, replaced by potassium in the neutralization with alkali, are placed first.

The synthesized heterotriacids are more or less powerful oxidizing agents. The phospho-, silicomolybdovanadic and phosphomolybdotungstic I and II acids have a real oxidation potential, found within the limits 0.77-0.64 V. The stability of the reduction products is greater the lower the tungsten content.

SUMMARY

1. By employing the potentiometric titration method, using potassium hydroxide solution and a glass electrode, and also by measuring the conductivity and pH values of the water solutions, it was shown that the basicity of heterotriacids, containing vanadium in the nature of addenda, is equal to five and six.

2. The melting points of the crystallohydrates of the heterotriacids were determined, and it was shown that they depend on the nature of the heteropolyanions.

3. The possibility of using the synthesized heterotriacids as oxidizing agents and as precipitants in certain analytical reactions was shown.

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STUDY OF THE REACTIONS OF POLYTHIONATES WITH THE AID OF LABELED SULFUR

III. REACTION OF THE HEXATHIONATE

V. A. Lunenok-Burmakina

In the studies of A. I. Brodsky and R. K. Eremenko [1, 2], with the aid of the radioactive sulfur isotope, the mechanism of some of the reactions for the formation and decomposition of the tri-, tetra- and pentathionates was elucidated. In this study the reactions for the formation and decomposition of the hexathionate were studied in the same manner.

Even as early as 1888 Debus [3] indicated the existence of hexathionic acid in Wackenroder's liquid, but it was only in 1927 that Weitz [4] was the first to isolate its potassium salt by pouring a solution of potassium thiosulfate and nitrite into cooled hydrochloric acid. The properties of the obtained salt were studied by Weitz. A second method for obtaining the hexathionate from sulfur chloride and thiosulfate was developed by Goehring [5].

In the present paper we studied the mechanism of the reactions for the formation of potassium hexathionate by both methods, and also the reactions for its decomposition with potassium cyanide, potassium sulfite and ammonia. The method for the decomposition of the hexathionate with potassium cyanide, separation of the reaction products and measurement of the radioactivity was described earlier [1, 2].

Preparation of Potassium Hexathionate From the Thiosulfate, Nitrite and Hydrochloric Acid [4, 6]

To a mixture of 67 ml of hydrochloric acid and 33 ml of water, cooled to $-40°$, was added a solution of 30 g of labeled potassium thiosulfate* and 4 g of potassium nitrite in 30 ml of water. The bulk of the nitrogen oxides separated in several minutes; their final removal was accomplished by blowing nitrogen through the solution. The deposited potassium chloride was filtered, and the filtrate was evaporated in vacuo at 25-30°. The obtained product, containing the hexathionate, chloride and sulfate of potassium, was transferred to a glass filter, washed with a small amount of water, then with alcohol, and air-dried. For final purification the hexathionate was recrystallized from 2N hydrochloric acid, washed with anhydrous alcohol, and dried on filter paper. Qualitative tests failed to show the presence of sulfite, sulfate, thiosulfate and trithionate as impurities in it.

About 0.6 g of the hexathionate was decomposed with potassium cyanide in accord with the stoichiometric equation (2). To prevent the formed thiosulfate from being decomposed by excess potassium cyanide to the thiocyanate and sulfate [7], the decomposition was run in dilute solutions.

The results of measuring the activity of the starting substances and of the hexathionate decomposition products are presented in Table 1.

The found distribution of the activity corresponds to the following total equation for the formation of the hexathionate:

$$4SSO_3^{--} + 2NO_2^- + 6H^+ = S_2(SSO_3)_2^{--} + 2HSO_3^- + 2NO + 2H_2O$$

* Labeled potassium thiosulfate was obtained by the method of [1].

and to the equation for its decomposition:

$$S_2(SSO_3)_2^{--} + 5CN^- + H_2O = SSO_3^{--} + 3CNS^- + SO_4^{--} + 2HCN,$$
$$SSO_3^{--} + 2Ag^+ + H_2O = Ag_2S + SO_4^{--} + 2H^+.$$

Reaction of the thiosulfate with nitrous acid also yields the tetrathionate [4, 8]. In a previous paper [2] it was shown that in the preparation of the tetrathionate from the thiosulfate and iodine the latter serves as the oxidizing agent, causing the union of two SSO_3^{--} groups through the S-S bond between the sulfide sulfur atoms. It must be surmised that the NO_2^- ion in acid solution plays the same role, and that the tetrathionate is also formed in reaction (1), which, replacing the sulfite ions by thiosulfate ions, is then changed in sequence into the penta- and hexathionate:

$$2SSO_3^{--} + 2NO_2^- + 4H^+ = \begin{array}{c} SSO_3^- \\ | \\ SSO_3^- \end{array} + 2NO + 2H_2O,$$

$$\begin{array}{c} SSO_3^- \\ | \\ SSO_3^- \end{array} + SSO_3^{--} + H^+ = S\begin{array}{l} \diagup SSO_3^- \\ \diagdown SSO_3^- \end{array} + HSO_3^-,$$

$$S\begin{array}{l} \diagup SSO_3^- \\ \diagdown SSO_3^- \end{array} + SSO_3^{--} + H^+ = \begin{array}{c} SSSO_3^- \\ | \\ SSSO_3^- \end{array} + HSO_3^-.$$

The sum of equations (3)-(5) gives (1). The presented equations correspond to the one found in earlier studies [1, 2, 9] for the mechanism of the reactions of the lower polythionates, in accord with which these reactions are accomplished by the method of exchanging whole sulfite and thiosulfate groups; here during the time of these transformations the sulfide and sulfite sulfur atoms retain their valence state.

TABLE 1

Hexathionate From SSO_3^{--}, NO_2^- and HCl

Expt. no.	Specific activity of the sulfur in imp/mg • min						Activity ratios				
	initial sulfur A	initial thiosulfate B	hexathionate C	decomp. of the hexathionate: thiosulfate D	decomp. of the hexathionate: thiocyanate E	decomp. of the final thiosulfate Ag_2S F	A/B	A/C	A/D	A/E	A/F
1	1475	720	—	700	1450	1500	2.05	—	2.11	1.02	0.98
2	1005	485	620	445	1015	990	2.07	1.62	2.26	0.99	1.02

Remarks. 1. In all of the experiments the sulfate isolated as the decomposition result of the final thiosulfate was inactive. 2. The average values of measuring the activity of two to three individual samples are given in the Table.

Hexathionate From Sulfur Chloride and the Thiosulfate [5]

To a solution of 13.5 g of sulfur chloride in 50 ml of CCl_4, cooled to $-15°$, were simultaneously added a solution of 50 g of sodium thiosulfate in 75 ml of water and a mixture of 40 ml of concentrated hydrochloric acid with 40 ml of water, both previously cooled to 0°. The reaction mixture was shaken until it became

colorless, and then 7.5 ml of 0.6M ferric chloride solution was added to it. The water layer, containing the sodium hexathionate, was separated and evaporated in vacuo at 30° to a volume of 25 ml. The concentrate was filtered from sodium chloride and cooled to 0°. To it was added in drops, also cooled to 0°, a methanolic solution of KOH until the reaction was weakly acid. The deposited hexathionate was filtered, washed and recrystallized, the same as described above.

In the hexathionate, prepared by the described method, the radioactive label was introduced in two different positions, depending on whether active sulfur chloride or active sodium thiosulfate was taken for the synthesis.

Both of the hexathionate samples were decomposed with potassium cyanide. The results of measuring the activity are presented in Table 2.

As can be seen from the data in Table 2, the hexathionate had $\frac{1}{3}$ the activity of the initial sulfur. In the first case (Expts. 1-2) it was all concentrated in the thiocyanate, containing $\frac{2}{3}$ the activity of the initial sulfur. In the second case the sulfide atom of the thiosulfate decomposition has the activity of the initial sulfur, and the thiocyanate only $\frac{1}{3}$ of it.

The obtained distribution of the activity corresponds to the following mechanism for the reaction. Sulfur chloride, as the chloride of the unstable thiosulfurous acid, gives this acid on hydrolysis, the hydroxyl groups of which are quickly replaced by thiosulfate radicals:

$$S_2Cl_2 + 2H_2O = S_2(OH)_2 + 2H^+ + 2Cl^-,$$
$$S_2(OH)_2 + 2SSO_3^{--} = S_2(SSO_3)_2^{--} + 2OH^-.$$

The decomposition of the hexathionate proceeds by the reaction

$$S_2(SSO_3)_2^{--} + 5CN^- + H_2O = SSO_3^{--} + 2CNS^- + CNS^- + SO_4^{--} + 2HCN.$$

TABLE 2*

Expt. no.	Specific activity of the sulfur in impulses/mg • min): initial sulfur A	initial thiosulfate B	hexathionate C	decomp. of the hexathionate: thiosulfate D	decomp. of the hexathionate: thiocyanate E	decomp. of the final thiosulfate Ag_2S F	Activity ratios: A/B	A/C	A/D	A/E	A/F
1	305	0	100	0	205	0	—	3.05	—	1.43	—
2	305	0	100	0	200	0	—	3.05	—	1.53	—
3	1670	855	550	820	560	1605	1.95	3.04	2.04	2.98	1.04

* See the remarks to Table 1.

To obtain the hexathionate from S_2Cl_2 and SSO_3^{--} and its decomposition with cyanide the equations are rewritten as follows:

$$S_2Cl_2 + 2H_2O = S_2(OH)_2 + 2H^+ + 2Cl^-,$$

$$S_2(OH)_2 + 2SSO_3^{--} = S_2(SSO_3)_2^{--} + 2OH^-,$$

$$S_2(SSO_3)_2^{--} + 5CN^- + H_2O = SSO_3^{--} + CNS^- + 2CNS^{--} + SO_4^{--} + 2HCN.$$

As a result, this reaction is also accomplished by the method of transposing whole thiosulfate groups.

The obtained results also show that the radioactive label, introduced into the hexathionate, then remains unchanged, i.e. there is no exchange between the sulfide atoms of the sulfur chain in the polythionate. This permits obtaining the higher polythionates, in which not all of the sulfide sulfur atoms are labeled, and only a part of them, which can serve to facilitate an elucidation of the complex reaction mechanisms of the higher polythionates.

Decomposition of the Hexathionate With Ammonia and With Sulfite

A characteristic reaction of the hexathionate, serving for its qualitative determination, is its reaction with ammonia; here the hexathionate is immediately decomposed with the liberation of sulfur. Statements exist that the reaction proceeds with the formation of the tetrathionate and sulfur [4], but there is a lack of information on its mechanism.

Several samples of the hexathionate, obtained by all of the above-described methods, were subjected to decomposition by ammonia:

$$S_2(SSO_3)_2^{--} \quad (I); \qquad S_2(SSO_3)_2^{--} \quad (II); \qquad S_2(SSO_3)_2^{--} \quad (III)$$

To a weighed sample of the hexathionate (1-0.5 g), dissolved in a small amount of water was added 5-2 ml of ammonia, and the deposited sulfur was filtered, thoroughly washed with water, and recrystallized from benzene.

In the decomposition of hexathionate (I) the radioactivity of the deposited sulfur was equal to the initial activity. The activity of the sulfur from the decomposition of hexathionate (II) proved to be somewhat less (about 70%) than the activity of the initial sulfur. The other decomposition products of the hexathionate were also isolated by us. For this the solution of the ammonia-decomposed hexathionate, after filtering off the sulfur, was evaporated on the water bath. A white powder was obtained, consisting of the thiosulfate and the tetrathionate. The sulfide sulfur of these products, depositing as Ag_2S when silver nitrate was added, contained about 30% of the activity of the initial sulfur.

In the decomposition of hexathionate (III) the radioactivity of the deposited sulfur was small, whereas considerable activity (somewhat less than the initial) was observed in the Ag_2S from the decomposition of the thiosulfate and the tetrathionate.

The activity of the sulfur, obtained as a deposit when ammonia is added to a solution of hexathionate (III), becomes greater the longer the contact time of the liberated sulfur with the decomposition products. Thus, if the sulfur was filtered in 10 minutes after the ammonia addition, then its activity was equal to 10% of the initial. In this experiment the activity of the sulfur in the sulfide atom of the decomposition products was equal to 90% of the radioactivity of the initial sulfur. When the time of the experiment was increased to 20 hours the activity of the deposited sulfur increased to 20%, and the activity of the Ag_2S correspondingly dropped to 80% of the initial.

The obtained data can be explained as being due to the fact that two central sulfur atoms are liberated in the decomposition of the hexathionate with ammonia, in which connection this process is accompanied by the exchange of the liberated sulfur with the sulfide sulfur of the thiosulfate.

The reaction for the decomposition of the hexathionate with sulfite proceeds in accord with the total equation

$$K_2S_6O_6 + 3K_2SO_3 = K_2S_3O_6 + 3K_2S_2O_3.$$

Proceeding from the representations, developed in previous studies [1, 2, 9] and supported in the present investigation, in accord with which the reactions of polythionates proceed by way of transfer of sulfite and thiosulfate groups, the following mechanism can be postulated for the given reaction:

$$K_2S_6O_6 + K_2SO_3 = K_2S_5O_6 + K_2S_2O_3,$$
$$K_2S_5O_6 + K_2SO_3 = K_2S_4O_6 + K_2S_2O_3,$$
$$K_2S_4O_6 + K_2SO_3 = K_2S_3O_6 + K_2S_2O_3.$$

If the reaction is run with hexathionate (II), then with such a sequence the activity in the decomposition products would be distributed in the following manner: $^{-}O_3\overset{3/4}{S}SO_3^{-}$ and $\overset{8/12}{S}SO_3^{--}$, where the initial activity of the sulfur is taken as unity. In the case of hexathionate (III) the distribution of the activity should be $^{-}O_3\overset{1/4}{S}SO_3^{-}$ and $\overset{7/12}{S}SO_3^{--}$. However, since the thiosulfate groups of polythionates show very rapid exchange with thiosulfate [9], then the indicated distribution could have been observed only in the case where the reaction rate was substantially higher than the exchange rate.

Two experiments were run with hexathionate (II) and (III). Equivalent amounts of hexathionate and sulfite were dissolved in water. The bulk of the formed thiosulfate was precipitated with barium chloride, while the remainder, interfering with the isolation of the sulfide sulfur of the trithionate as CuS, was converted by iodine into the tetrathionate. Analysis revealed that the radioactivity of the sulfide atoms of the trithionate and thiosulfate was the same and equal to one-half the activity of the initial sulfur. The found distribution of the activity testifies to the fact that complete equalization of the activities of all of the sulfide sulfur atoms occurs during the decomposition process as the result of the exchange of thiosulfate groups.

The obtained data are in accord with the representations of D. I. Mendeleev relative to the polythionates [10, 11].

In conclusion I wish to thank A. I. Brodsky for recommending this subject and for his assistance in the execution of the work.

SUMMARY

1. With the aid of labeled sulfur we studied the reactions for the formation of hexathionate from thiosulfate, nitrite and hydrochloric acid, and from sulfur chloride and thiosulfate, and also the reactions for the decomposition of hexathionate with potassium cyanide, ammonia and potassium sulfite. Probable mechanisms for these reactions were proposed.

2. The absence of exchange in the polysulfide chain of the sulfur atoms of the polythionate was established. This permits obtaining the higher polythionates, in which not all of the sulfide sulfur atoms are labeled, but only a part of them, which can facilitate an elucidation of the complex reaction mechanisms of the higher polythionates.

3. The data of this study support the earlier derived conclusions relative to the mechanism of the reactions for the formation and mutual transformations of the polythionates via the exchange of sulfite and thiosulfate groups, and relative to the structure of polythionates from unbranched polysulfide chains with SO_3 groups on the ends. This, as was indicated earlier, is in accord with the representations of D. I. Mendeleev.

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APPLICATION OF CHROMATOGRAPHY TO A STUDY OF THE REACTIONS OF DIMETHYLGLYOXIME WITH METAL CATIONS. II.

A. M. Gurvich

Organic reagents, capable of forming complexes with metal cations, were first used as sorbents for inorganic chromatography by Erlenmeyer and coworkers [1], who used o-hydroxyquinoline for this purpose. Later other organic reagents, including dimethylglyoxime (H_2Dm), were used as chromatographing sorbents by a number of investigators [2, 3].

T. B. Gapon and E. N. Gapon formulated the principles of precipitation chromatography [4], combining under this term all of the cases of chromatographic separation, based on a difference in the solubility products of the compounds, formed by the components of the mixture with the chemosorbent, entering into the composition of the column. To assure a sufficiently rapid and uniform filtration of the solution through such a column the chemosorbent was mixed with a carrier, inert with respect to both the reactants and the reaction products.

In the previous communication [5] we discussed the results of using a column of active carbon for this purpose, into which the H_2Dm was introduced by the method of absorbing it from its saturated water solutions on carbon, and also the results of using a column composed of a mixture of H_2Dm and carbon, placed over a layer of pure carbon, which we had already used earlier for the purification of zinc and cadmium salts from traces of Ni, Co, Cu and Fe [6], and for the separation of Ni and Co [7]. In the given case the sorbent is the carrier, capable of adsorbing the soluble compounds formed in the column from the metals and H_2Dm, which permits separating the metals from the substances that fail to react with H_2Dm, and also from each other. Evidently, in precipitation chromatography the adsorption phenomena always accompany the separation process in varying degree; however, in the examined case they are not a secondary phenomenon, but the factor that determines the possibility of separation.

The ability of metal cations to be separated in the described type of columns, which we call adsorption-complex forming (in the particular case, carbon-dimethylglyoxime), can be used to determine the relative stability of the compounds formed in the column.

Isolated incomplete data exist in the literature on the stability of the complexes of H_2Dm with divalent metals. A. K. Babko and P. B. Mikhelson found [8] that the solubility product of $Ni(HDm)_2$ is $2 \cdot 10^{-25}$. According to the data of A. K. Babko and L. I. Dubovenko [9], the dissociation constant of $Fe(HDm)_2$ is $2 \cdot 10^{-13}$. Any quantitative data on the stability of $Cu(HDm)_2$ is absent in the literature. Some investigators believe [10] this compound to be less stable than $Ni(HDm)_2$. A. K. Babko and M. V. Korotun [11] assign a value of $(0.8\text{-}1.5) \cdot 10^{-10}$ to the dissociation constant of the complex $Cu(HDm)^+$, the formation of which they postulate occurs in weakly acid (pH ≈4.5) medium. From this fact, that when Ni^{++} is added to a mixture of Co^{++} and H_2Dm, in which the Co^{++} is found in slight excess, a precipitate of $Ni(HDm)_2$ is not obtained, Babko and Korotun conclude [12] that $Co(HDm)_2$, the formation of which they postulate under these conditions, is more stable than $Ni(HDm)_2$. For the dissociation constant of the compound $[Co(HDm)_2 \cdot 2H_2O]$, which, in the opinion of L. S. Nadezhina [13], is formed in alkaline medium in the presence of Na_2SnO_2, the author gives a value of $(3.67 \pm 0.5) \cdot 10^{-11}$.

We had shown [5] that in a carbon-dimethylglyoxime column the cations Cu^{++}, Ni^{++}, Co^{++} and Fe^{++} form compounds of general formula $Me(HDm)_2$. Evidently, from a mixture of two cations the first to react with H_2Dm, forming the upper zone of the chromatogram, will be the cation (Me_I) that under other conditions constant gives a compound that is characterized by a lower value for the dissociation constant. During continuous filtration of the solution through the column this cation will displace the second cation (Me_{II}) from its compound with H_2Dm:

$$Me_I^{++} + Me_{II}(HDm)_2 \rightleftharpoons Me_I(HDm)_2 + Me_{II}^{++}, \quad (1)$$

in view of the fact that the equilibrium constant of this reaction

$$K_1 = \frac{K_{\text{dissociation } Me_{II}(HDm)_2}}{K_{\text{dissociation } Me_I(HDm)_2}} > 1.$$

In view of the fact that all of the compounds of the $Me(HDm)_2$ type are held very tenaciously on a carbon surface, a slight difference in their absorption ability does not influence the order in which the cations pass into the filtrate. Due to the presence of a layer of pure carbon of definite length in the lower part of the column, neither H_2Dm nor its compound pass into the filtrate even when large volumes of solutions are passed, exceeding by a hundred times the volume of the sorbent. A complicating circumstance is the dissimilar adsorption of cations on carbon; however, the order in which cations pass through a carbon column does not coincide for the most part with the order of their passage through a carbon-dimethylglyoxime column. With the aid of the frontal analysis method this makes it possible to compare the relative stability of the compounds formed in the column.

EXPERIMENTAL

It was shown by preliminary experiments that the amount of carbon in the lower layer of the column should be not less than half its amount in the upper layer. The column that we used consisted of 1 g of carbon in the lower layer and a mixture of 1.5 g of carbon and 0.15 g of H_2Dm in the upper layer. The column diameter was 10-12 mm. The characteristics of the carbon had been described by us earlier [5, 6]. Its preparation for experiment did not differ from that described in [6]. The carbon was sifted into the column in the air-dried state (moisture ~ 6%). The carbon-H_2Dm misture was also prepared and sifted into the column in the dry state. The assembled column was fed with water.

Studied pair of cations	Sequence of sorption (in dimin. order): in carbon-dimethylglyoxime	Sequence of sorption (in dimin. order): in carbon column
Co^{++} & Fe^{++} .	Co^{++} — Fe^{++}	Fe^{++} — Co^{++}
Ni^{++} & Co^{++} .	Ni^{++} — Co^{++}	Ni^{++}, Co^{++}
Cu^{++} & Ni^{++} .	Cu^{++} — Ni^{++}	Cu^{++} — Ni^{++}
Cu^{++} & Fe^{++} .	—	Cu^{++} — Fe^{++}

The separation of paired mixtures of equinormal solutions of Ni^{++}, Co^{++}, Cu^{++} and Fe^{++} salts (chlorides and sulfates) was studied by us. The total concentration of the cations was varied in the limits of 0.02-0.06N. The pH of the solutions, containing Fe^{++}, was 4.1-4.3; for the other solutions it ranged in the limits 5-6. No foreign substances were added to the solutions. As had already been mentioned, to a certain degree the carbon played the role of pH regulator, adsorbing (both hydrolytically and molecularly) the acid, and in the experiments with Fe^{++} it also played the role of reducing agent. No less than five experiments were performed for each pair of cations. In addition, the separation of the same pair of cations on a carbon column was studied, composed of 2.5 g of active carbon, which was prepared in the same manner as the carbon-dimethylglyoxime column. The filtrate was collected in 2 ml portions and analyzed. The experimental results are presented in the form of a table, in which the cations that show separation are separated from each other by a hyphen, and those that do not show separation by a comma.

Since the sorption order of the pair $Cu^{++} - Ni^{++}$ coincided in both columns, some additional experiments were run, in which the Cu^{++} concentration was more than 8 times the Ni^{++} concentration. But also in these experiments the first to appear in the filtrate was the nickel. In addition, the introduction of H_2Dm into the carbon column greatly improved the separation of these cations.

The use of carbon, saturated with acid [5], as the adsorbent does not give any advantages in the given case. On the contrary, simultaneously with impairment in the separation of cations on such a carbon, due to the loss of its capacity for hydrolytic adsorption (the capacity for the physical adsorption of heavy metal salts and mineral acids is retained), the separation conditioned by the influence of H_2Dm is also impaired for the same reason: the absorption of the acid liberated in the reaction of the cations with H_2Dm is decreased.

DISCUSSION OF RESULTS

From the presented data it can be seen that the investigated cations can be arranged in the following sequence in the order of diminishing stability of the intracomplex compounds formed by them in a carbon-dimethylglyoxime column:

$$Cu^{++} > Ni^{++} > Co^{++} > Fe^{++}. \qquad (2)$$

This conclusion, made by us on the basis of comparing the sorption order of cations on carbon-dimethylglyoxime and carbon columns, is also supported by other observations.

It is evident that the more stable the $Me(HDm)_2$ compound, the more, with other conditions constant, the reaction between the metal cation Me^{++} and H_2Dm is shifted toward the formation of the complex, and the greater

$$Me^{++} + 2H_2Dm \rightleftharpoons Me(HDm)_2 + 2H^+ \qquad (3)$$

is the stability of the latter to the influence of acid.

Consequently, it follows that the more to the left that a cation stands in series (2), the more completely it is bound in a carbon-dimethylglyoxime column, and the lower the value of the lower pH limit, where under the given conditions reaction is practically complete.

Actually, as can be seen from the data of [5], the cation concentration in the filtrate after running the reaction in the column under similar conditions increases from Cu^{++} to Fe^{++} in the same sequence as in (2), where, as postulated by us, the stability of the corresponding complex compounds decreases. We will mention that the arrangement order of the examined cations is the same in the series on the degree of removing $ZnSO_4$ and $CdSO_4$ solutions from them on a carbon-dimethylglyoxime column in the presence of sodium acetate (pH 5.8-6.0) [6]. From the slope of the curves (Figure) for increase in cation concentration in the filtrates of a series of consecutive experiments made to determine the structure of the compounds of metals with H_2Dm, run for each cation on the same column by the method described in [5], the cations form the same sequence (2) as is observed in determining the order of their passage into the filtrate.

Based on the stability of the intracomplex compounds formed by them with H_2Dm, the cation series found by us coincides with the series having general significance for the complexes of these metals with various addenda [14, 15] and expressed with especial distinctness for the addenda, forming bonds with the central atom through a nitrogen atom, which can be assumed for compounds of the $Me(HDm)_2$ type [16].

Series (2) determines the lower limit of the dissociation constants of $Cu(HDm)_2$ and the upper and lower limits of the dissociation constants of $Co(HDm)_2$, since the values of the solubility product of $Ni(HDm)_2$ and of the dissociation constants of $Fe(HDm)_2$ are known [8, 9].

In passing we will mention that the order observed by us for the passage of cations into the filtrate when the solutions of their salts are passed through a carbon column, and specifically (Table) agrees with the adsorp-

$$Cu^{++} > Fe^{++} > Ni^{++} = Co^{++} \qquad (4)$$

tion order of these cations on carbon, found by N. A. Shilov and L. K. Lepin [17] from experiments run under static conditions.

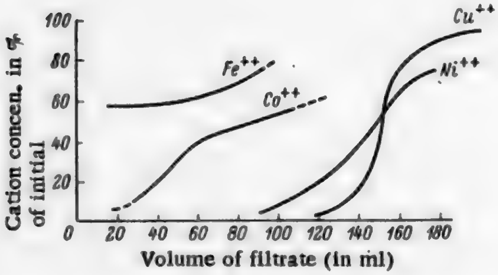
The chromatographic method described by us for determining the relative stability of complex compounds, besides the dimethylglyoximines, can also be applied to compounds of metals with other organic reagents having a low solubility in water.

Thus, on columns composed of a mixture of carbon and α-nitroso-β-naphthol, which, as is known, is capable of reacting with the same cations, the dimethylglyoximines which had been studied by us [18, 19], forming with them, depending on the conditions, either insoluble or soluble compounds, we obtained the following order:

$$Cu^{++} > Ni^{++} > Fe^{++}, \qquad (5)$$

in which the stability of the corresponding α-nitroso-β-naphtholates decreases from left to right.

Finally, it should be borne in mind that in such adsorption-complex forming chromatographic columns the reaction can proceed somewhat differently than in solution, due to the stabilization of the primary metastable reaction products in their adsorption by carbon or as the result of a shift in the equilibrium toward the side of forming the least polar complexes [5].



Curves for the increase in cation concentration in the filtrates of a series of consecutive experiments on the determination of the structure of compounds of metals with dimethylglyoxime.
(The carbon was treated with acid in accord with the data of [5], and the dimethylglyoxime was adsorbed on carbon).

The discussed method gives a separation picture that is the opposite of the one observed in ion-exchange chromatography with complex-forming elution [20]: if in the washing of ion-exchange columns with solutions of organic reagents, capable of forming complex compounds with the metals being separated, the first cation to pass into the filtrate is the one that forms the most stable compound, then in the chromatographing on adsorption-complex forming columns of the discussed type it is the cation forming the least stable compound that is the first to pass into the filtrate. A condition for the use of complex-formation elution is a more or less substantial solubility of the proper reagent; on the contrary, a condition for the use of adsorption-complex forming columns is a low solubility of the reagent; here in the last case the reagent, readily adsorbed on the carrier, remains in the column and does not contaminate the solutions of the cations being separated. We have already made use of this circumstance in the purification of cobalt salts from nickel impurities [7]. Complex-formation elution is a secondary operation, following after the primary chromatogram had been obtained; the method of adsorption-complex forming chromatographic separation is accomplished as the result of using only one operation – filtration of the solution of the substances being separated through a column. This makes it possible to use the examined method in the solution of a number of problems on an industrial scale.

To study the reactions of cations with H_2Dm, in addition to the carbon-dimethylglyoxime columns, those composed of a mixture of aluminum oxide and H_2Dm can be used, which prior to chromatographing should be impregnated with water [7]. Since under these conditions the compounds of metals with H_2Dm, formed in the column, are adsorbed (although weakly) by aluminum oxide, then up to a certain degree the phenomena observed in such columns are comparable with the phenomena occurring in carbon-dimethylglyoxime columns. Thus, a nickel displaces cobalt from its compound with H_2Dm [7], although in solution this is not observed [12]. But in these columns, in contrast to the columns with carbon, the separation of cations is determined not only by the stability of the complex compounds, but also by their ability to be adsorbed on Al_2O_3. This leads to transpositions in the adsorption series. Thus, the brown zone of iron dimethylglyoximine (II) shows up between the nickel and cobalt zones. In addition, in view of the already mentioned influence of adsorption on the course of complex formation with participation of H_2Dm the reaction in the column with aluminum oxide, being a heteropolar adsorbent, can proceed somewhat differently than in a carbon-dimethylglyoxime column, where the carrier represents a homeopolar adsorbent.

Aluminum oxide is a regulator of the pH, adsorbing the acid that is liberated during the reaction process. But this does not exhaust its influence as a chemically active agent: it can also cause some secondary reactions to appear. The process, taking place in the column, depends on the previous treatment of the Al_2O_3. The shape of the chromatograms on an acid aluminum oxide and their change with time differ from those obtained on an alkaline aluminum oxide. This refers, for example, to the chromatograms of Co^{++} and Fe^{++}. The fact that H_2Dm does not show substantial adsorption on Al_2O_3 from water solutions (for which reason the lower layer of pure carrier is superfluous in such columns) also plays a role. When solutions are poured into the column the

H_2Dm salts partially dissolve in them, and the compound, formed in the solution, where reaction can proceed differently than in the column [5], is adsorbed on the Al_2O_3. This leads to the situation that the upper portion of the chromatogram can have a different appearance from the remainder of the chromatogram, which is observed in the case of Cu^{++}, and also of Co^{++}, in which connection this phenomenon is augmented due to stratification of the Al_2O_3 and H_2Dm in the upper portion of the column during packing; consequently it is expedient to remove the upper layer of the column after wetting.

The complex appearance of the chromatograms is explained in some cases by the comparatively low solubility of the compounds formed in the column. Thus $Cu(HDm)_2$, the solubility of which in water at 22° is determined as being $6 \cdot 10^{-3}$ gram-mole/ liter (0.17%) [11], gives in such a column a series of thickly situated dark-gray spots on a brownish-gray zone as the ground, descending below the zone boundary of the spots.

Frequently the appearance of the chromatograms of two cations cannot be explained by a simple superimposition of the zones of the complex compounds, formed in the column by each cation separately. This was also mentioned by F. M. Shemyakin and E. S. Mitselovsky [21] in their chromatographing on o-hydroxyquinoline.

With all of the complexity of the reactions and process of separation in a column composed of a mixture of Al_2O_3 and H_2Dm, still such a column can be useful in view of the fact that the chromatogram on it is observed visually. The analytical use of such a column had been discussed by us earlier [7].

A series of data can be obtained in the adsorption of compounds of cations with H_2Dm, obtained in solution, on a column of aluminum oxide impregnated with water. Thus the brown solution, formed in the treatment of $Ni(HDm)_2$ precipitate with $CuSO_4$ solution, gives a green and a sky-blue zone on the Al_2O_3 column. The green zone evidently belongs to the complex to which Babko and Korotun [11] assign the formula $Cu(HDm)^+$; the sky-blue zone was formed by the unreacted copper. A green zone is formed in the chromatographing of the solution, obtained by the reaction of $CuSO_4$ with solid H_2Dm in weakly acid medium, after separating the solution from the precipitate and adding sodium acetate to it. A solution of the black compound $Cu(HDm)_2$, isolated by Chugaev [22], gives a brownish-gray zone on aluminum oxide. As a result, the chromatographic experiments on Al_2O_3 support the possibility of forming two compounds of Cu^{++} with H_2Dm in weakly acid and neutral medium, depending on the concentration conditions and the pH.

SUMMARY

1. A method was developed for determining the relative stability of single-type complex compounds of metals with an organic reagent showing good adsorption on carbon, consisting in the determination of the order in which the metals pass into the filtrate during the frontal chromatographic analysis of aqueous solutions of their salts on columns composed of a mixture of carbon and the organic reagent, situated above a layer of pure carbon.

2. It was established that the metals can be arranged in the following sequence in the order of diminishing stability of their intracomplex compounds with dimethylglyoxime of general formula $Me(HDm)_2$:

$$Cu^{++} > Ni^{++} > Co^{++} > Fe^{++}.$$

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VISCOSITY OF BINARY SYSTEMS WITH CHLORAL. V.

V. V. Udovenko and R. I. Khomenko

To clarify the character of the reaction of chloral with esters and ethers, we studied the viscosity of the following systems: chloral – ethyl formate, chloral – ethyl acetate, chloral – ethyl ether, chloral – anisole and chloral – acetoacetic ester. The viscosity is constant in the first four systems while with chloral – acetoacetic ester it changes with time; due to this, mixtures in the latter system were sealed in ampules and heated on a water bath for three weeks before measuring the viscosity. In the other cases, the viscosity was measured immediately after the mixtures were prepared. The materials required for the work were purified by preliminary drying and then careful distillation. The mixtures were prepared from fractions having the following boiling points: ethyl formate 51.2° at 718 mm, ethyl acetate 75.0° at 725 mm, ethyl ether 33.2° at 735 mm, anisole 152.0° at 729 mm and acetoacetic ester 67.0° at 10.5 mm.

TABLE 1

The System Chloral – Ethyl Formate

Chloral content (mole %)	Viscosity			Density		
	25°	35°	50°	25°	35°	50°
0.00	0.4090	0.3633	0.3192	0.9175	0.9060	0.8889
9.63	0.5272	0.4687	0.4034	0.9971	0.9823	0.9629
26.28	0.6835	0.6087	0.5164	1.1235	1.1108	1.0902
34.80	0.7353	0.6482	0.5508	1.1757	1.1600	1.1404
50.15	0.8523	0.7462	0.6260	1.2686	1.2553	1.2330
64.09	0.9207	0.8000	0.6710	1.3457	1.3286	1.3059
74.34	0.9827	0.8530	0.7260	1.4013	1.3708	1.3477
87.27	1.0304	0.9164	0.7589	1.4533	1.4368	1.4128
100.00	1.0552	0.9017	0.7641	1.5013	1.4859	1.4603

In the system chloral – ethyl formate the viscosity was measured at temperatures of 25, 35 and 50°. The results of viscosity and density measurements are given in Table 1. The viscosity isotherms are concave towards the composition axis.

In the system chloral – ethyl acetate the viscosity was measured at temperatures of 25, 50 and 75°. The results of viscosity and density measurements are given in Table 2. The viscosity isotherms have an S shape.

In the system chloral – ethyl ether the viscosity was measured at 25 and 35°. The results of viscosity and density measurements are given in Table 3. The viscosity isotherms are straight lines.

In the system chloral – anisole the viscosity was measured at temperatures of 25, 50 and 75°. The results of viscosity and density measurements are given in Table 4. The viscosity isotherm at 25° passes through a slight maximum which is situated close to 83 mole % of chloral. At temperatures of 50 and 75°, the maximum disappears and in this range of concentrations the viscosity isotherms become concave towards the composition axis.

TABLE 2

The System Chloral–Ethyl Acetate

Chloral content (mole %)	Viscosity			Density		
	25°	50°	75°	25°	50°	75°
0.00	0.4377	0.3435	0.2825	0.8976	0.8668	0.8448
9.53	0.4807	0.3778	0.3077	0.9555	0.9244	0.8953
20.23	0.5348	0.4206	0.3395	1.0230	0.9915	0.9620
29.01	0.5960	0.4576	0.3671	1.0754	1.0445	1.0135
39.47	0.6491	0.4963	0.3978	1.1394	1.1055	1.0706
49.10	0.7355	0.5518	0.4370	1.1998	1.1650	1.1292
59.82	0.8139	0.6033	0.4618	1.2700	1.2333	1.2019
69.72	0.9183	0.6703	0.5280	1.3301	1.2927	1.2540
81.13	1.0005	0.7285	0.5602	1.3990	1.3601	1.3202
89.92	1.0347	0.7720	0.5899	1.4491	1.4089	1.3707
100.00	1.0552	0.7641	0.5895	1.5013	1.4603	1.4186

TABLE 3

The System Chloral–Ethyl Ether

Chloral content (mole %)	Viscosity		Density	
	25°	35°	25°	35°
0.00	0.2357	0.2203	0.7049	0.6942
9.72	0.3229	0.2957	0.8619	0.8489
19.81	0.4119	0.3734	0.9856	0.9725
29.94	0.4946	0.4545	1.0941	1.0796
39.92	0.5710	0.5131	1.1746	1.1590
50.26	0.6528	0.5857	1.2514	1.2365
59.97	0.7314	0.6440	1.3161	1.3000
70.25	0.8111	0.7286	1.3752	2.3603
80.06	0.8889	0.7893	1.4214	1.4047
89.91	0.9692	0.8449	1.4666	1.4439
100.00	1.0552	0.9017	1.5013	1.4859

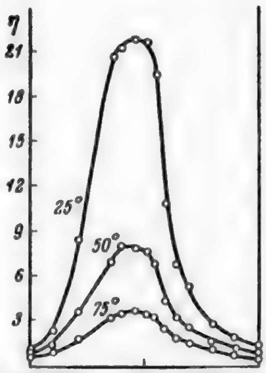
TABLE 4

The System Chloral–Anisole

Chloral content (mole %)	Viscosity			Density		
	25°	50°	75°	25°	50°	75°
0.00	1.0121	0.7135	0.5443	0.9907	0.9683	0.9452
10.22	1.0104	0.7191	0.5483	1.0375	1.0143	0.9894
19.96	1.0135	0.7212	0.5517	1.0875	1.0612	1.0361
28.94	1.0172	0.7224	0.5533	1.1291	1.1003	1.0734
39.98	1.0192	0.7294	0.5538	1.1819	1.1549	1.1250
49.87	1.0267	0.7359	0.5668	1.2374	1.2004	1.1698
59.29	1.0343	0.7442	0.5726	1.2800	1.2487	1.2167
70.18	1.0479	0.7579	0.5800	1.3431	1.3091	1.2745
80.10	1.0679	0.7629	0.5822	1.4021	1.3614	1.3243
89.58	1.0633	0.7624	0.5828	1.4494	1.4072	1.3690
100.00	1.0552	0.7641	0.5885	1.5013	1.4603	1.4186

In the system chloral — acetoacetic ester the viscosity was measured at temperatures of 25, 50 and 75°. The results of the viscosity measurements are shown graphically in the figure and it may be seen from it that the viscosity isotherms go through a sharply expressed maximum at 54 mole % chloral, which is slightly displaced by an increase in temperature towards acetoacetic ester. The density isotherms have an S shape.

It is known that in the presence of pyridine, acetoacetic ester reacts with chloral [1, 2] and the compound formed is decomposed into chloral and acetoacetic ester by distillation in vacuum. Optical investigations of acetoacetic ester solutions in pyridine showed that similarly to alcohols acetoacetic ester reacted with pyridine at the hydroxyl group [3] (enol form). The reaction of chloral with acetoacetic ester also takes place at this hydroxyl group.



CCl_3CHO $CH_3COCH_2COOC_2H_5$

The data obtained on the viscosity of systems of chloral with esters and ethers seem to indicate that a reaction of the components takes place in all cases, although a sharply expressed reaction is observed only in the system chloral — acetoacetic ester.

In previous reports devoted to the study of the reaction of chloral with various organic materials, we showed that chloral formed chemical compounds by direct reaction only with those materials whose molecules contained a hydroxyl group. No such reaction can occur in the system chloral — ethyl acetate. The viscosity isotherms of this system have, however, an S shape. It is generally considered that such a form of viscosity isotherms appears in systems with chemical reaction of the components when the value of the viscosity of the compound formed lies between the values of the viscosity of the pure components [4]. Therefore, the question arises as to whether the S form of the viscosity isotherms appears only in systems with chemical reaction of components resulting in the formation of a definite compound or whether this condition is not obligatory. It seems to us that in the light of new experimental data it is necessary to examine the possibility of a wider interpretation of viscosity isotherms with an S form. However, this problem can be solved only when the nature of the bond and the character of the reaction of the components is clarified in the system chloral — ethyl acetate as well as in other systems of chloral with organic materials.

SUMMARY

1. The viscosity and density were studied for the systems chloral — ethyl formate at temperatures of 25, 35 and 50°, chloral — ethyl ether at 25 and 35° and the systems chloral — ethyl acetate, chloral — anisole and chloral — acetoacetic ester at 25, 50 and 75°.

2. Reaction of the components was established in all the systems studied; however, the reaction in the system chloral — acetoacetic ester was the only strongly expressed one and it was due to the presence of a hydroxyl group in the molecule of the latter.

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INVESTIGATIONS IN THE FIELD OF ALKOXYSILANES

VI. SYNTHESIS OF TETRAAROXYSILANES BY TRANSESTERIFICATION OF ETHYL SILICATE WITH PHENOLS*

M. G. Voronkov and G. B. Karpenko

The transesterification of ethyl silicate with aliphatic alcohols, proceeding according to the scheme:

$$Si(OC_2H_5)_4 + 4ROH \xrightarrow[OR^-]{H^+} Si(OR)_4 + 4C_2H_5OH,$$

has been studied quite thoroughly and is the most convenient method for synthesizing the higher tetraalkoxysilanes [6–12]. However, up to now hardly anyone has tried to apply this reaction to the synthesis of tetraaroxysilanes (which, in contrast to tetraalkoxysilanes, are hardly mentioned in the literature). Only Malatesta in one of his papers [9] mentions the possibility of the transesterification of $Si(OC_2H_5)_4$ with phenol in the presence of aluminum or sodium ethylate. Up to now, the aromatic esters of orthosilicic acid (mainly tetraphenoxysilane) were obtained by reacting phenols with silicon chloride [13–15], silicon sulfides [16, 17] or with an alloy of silicon and copper [18].

Hertkorn [13] showed that ethyl silicate is formed by heating tetraaroxysilanes with ethyl alcohol.

On this basis, it was concluded [19] that the alkoxy groups were bonded more firmly to the silicon atom than the aroxy. Therefore, it seemed likely that the reverse reaction of transesterification of ethyl silicate with phenols would be difficult to carry out.

It turned out that, contrary to this supposition, in the presence of the appropriate sodium phenate, ethyl silicate reacts smoothly with phenols of very different structures according to the above scheme. This reaction is a very simple and convenient method for synthesizing tetraaroxysilanes, and their yield is 70–85%.

It should be noted that phenols, especially those containingsubstituents which increase their acidity, react with ethyl silicate noticeably faster than with silicon chloride. Thus, for example, in contrast to the reaction between $Si(OC_2H_5)_4$ and p-chlorophenol, which proceeds readily, the reaction of the latter with $SiCl_4$ either does not occur [19] or proceeds extremely slowly [15].

It is interesting that ethyl salicylate does not undergo transesterification with ethyl silicate in the presence of either an alkali or acid catalyst. On the contrary, almost the whole theoretical amount of ethyl alcohol was distilled off in the reaction of ethyl silicate with p-nitrophenol in the presence of the sodium derivative of the latter. However, the reaction product was a hard, black, insoluble and nonvolatile polymer.

The aromatic esters of orthosilicic acid synthesized by us by the transesterification of ethyl silicate with phenols are summarized in the table. We obtained tetracyclohexoxy-, tetracyclopentoxy- and tetrabenzoxysilane by an analogous method.

Tetraaroxysilanes are colorless, readily hydrolized crystalline materials of viscous liquids, which dissolve readily in the usual organic solvents and usually crystallize badly from them. It should be noted that the crystalline phenols give tetraaroxysilanes which are usually solid at normal temperatures, while liquid aryl silicates are formed from liquid phenols.

*For preceding reports see [1–5].

Tetraaroxysilanes

R	Melting point	Boiling point at given pressure (mm)	n_D^{20}	% Si calculated	% Si found	Yield (in %)
C_6H_5	54°	236—237° (1)	—	7.05. 6.94	7.01	86
$2\text{-}CH_3C_6H_4$	—	247—248 (1)	1.5615	6.27. 6.21	6.15	69
$3\text{-}CH_3C_6H_4$	—	251—252 (1)	1.5587 *	6.13. 6.00	6.15	76
$4\text{-}CH_3C_6H_4$	71	257—258 (1)	—	6.02. 6.19	6.15	81
$2,4\text{-}(CH_3)_2C_6H_3$	97	292—293 (10)	—	5.68. 5.58	5.48	72
$3,4\text{-}(CH_3)_2C_6H_3$	51	303—304 (10)	—	5.62. 5.56	5.48	79
$2,5\text{-}(CH_3)_2C_6H_3$	—	295—296 (10)	1.5530	5.49. 5.58	5.48	75
$4\text{-}C_2H_5C_6H_4$	—	293—294 (10)		5.39. 5.45	5.48	80
$5\text{-}CH_3\text{-}2\text{-}(CH_3)_2CHC_6H_3$	48	265—270 (4)	—	4.58. 4.63	4.49	85
$2\text{-}CH_2{=}CHCH_2C_6H_4$	—	265—267 (1)	1.5640	5.08. 5.03	4.96	80
$4\text{-}ClC_6H_4$	80	285—286 (4)	—	5.19. 5.24	5.22	70
$C_6H_5CH_2$	33	259—260 (1)	—	6.05. 6.10	6.15	72
C_5H_9 (cyclopentyl)	—	195—196 (10)	1.4645	7.71. 7.81	7.62	88
C_6H_{11} (cyclohexyl)	92	236—237 (10)	—	6.65. 6.53	6.61	90

The statement found in the literature [20] that the orthosilicic esters of phenols are " as a rule, crystalline products" does not correspond to reality.

In most cases, the melting points found by us for tetraaroxysilanes are higher (by 1–5°) than those given in the literature. This is explained by the fact that for their recrystallization, we did not use alcohol (as did other authors) which transesterified with tetraaroxysilane, a reaction that Hertkorn had shown possible [13].

When illuminated by ultraviolet light, all the tetraaroxysilanes show a bright light blue, blue or violet fluorescence. We are the first to give the refractive indices of liquid tetraaroxysilanes.

EXPERIMENTAL

The ethyl silicate was prepared by distilling the technical product on a column over metallic sodium and had b.p. 168.0° (754 mm), n_D^{20} 1.3830.

The starting phenols and alcohols (chemically pure preparations) were distilled in vacuum immediately before introduction into the reaction. Their boiling points and melting points agreed well with the most reliable literature data.

Method of carrying out the syntheses. Into a distillation flask fitted with a 20 centimeter pear fractionating column was placed 41.6 g (0.2 moles) of ethyl silicate, 1 mole of the corresponding phenol (or alcohol) and 0.1–0.2 g of sodium. The reaction mixture was heated until we stopped distilling off ethyl alcohol, which usually came over at 77–79° in the theoretical amount (35–37 g). The residue in the flask was either distilled in vacuum at 0.5–1.5 mm (previous neutralization of the sodium phenate with an ether solution of HCl helped raise the yield somewhat) or purified by recrystallization after distilling off the excess phenol. The tetraaroxysilane, isolated by vacuum distillation of the crude material, was distilled a second time, after which it had the boiling point given in the table. The crystalline orthosilicic esters were recrystallized from a mixture of benzene and petroleum ether, carbon disulfide or dry acetone with precautions to exclude moisture from the air.

Analysis. The orthosilicic esters obtained were analyzed for silicon content by evaporating down samples of the material first with dilute and then with concentrated sulfuric acid with subsequent roasting at 900–1000°.

As an example we will give the description of the synthesis of tetra-(p-chlorophenoxy)-silane. Into a distillation flask with a pear condenser was placed 41.6 g (0.2 mole) of ethyl silicate, 0.2 g of sodium and 128.6 g (1 mole) of p-chlorophenol. The mixture was distilled. At 78–81°, 36.9 g (0.8 g mole) of ethyl alcohol came over, i. e., 100% of theoretical. Further distillation in vacuum gave 30 g of excess chlorophenol with b.p. 83–84° and 75.4 g (70%) of tetra- (p-chlorophenoxy)-silane with b.p. 272–275° (3 mm) which had the constants given in the table after a second distillation and recrystallization.

SUMMARY

It was shown that the transesterification of ethyl silicate with phenols in the presence of the appropriate sodium phenates resulted in the formation of tetraaroxysilanes in 70–85% yield. Eleven tetraaroxysilanes were synthesized by this method, as well as orthosilicic esters of cyclohexanol, cyclopentanol and benzyl alcohol.

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** Original Russian pagination. See C. B. translation.

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THE EFFECT OF INTERMOLECULAR INTERACTION ON BROMINATION IN THE BINARY SYSTEM BENZENE – NITROBENZENE

F. F. Cheshko, L. N. Novikova and O. I. Shevchenko

The existence of a nitrobenzene solvate of benzene was previously reported [1]. The solvation of benzene in a nitrobenzene solution is due to its polarization which was discovered by Holland and Le Fevre [2].

The effect of nitrobenzene in the binary system benzene-nitrobenzene is similar to the effect of a catalyst in a substitution reaction in the benzene ring [3]. A substitution reaction is initiated by the polarization of the components in a polar solvent as well as under the effect of catalysts. The benzene molecule is not polarized in a nonpolar solvent and therefore, does not tend towards intermolecular reaction.

We investigated the bromination of benzene in nitrobenzene, bromobenzene and tetrachloromethane solutions. The initiating effect of nitrobenzene on bromination is known only with respect to strongly polar materials, for example, indigo and not in solvents [3, 4]. The nitrobenzene molecule is a rigid dipole with a large moment $\mu = 4.24$ D [5]. The dipole moment of the bromobenzene molecule is less than $\mu = 1.54$ D [6]. The molecule of carbon tetrachloride is nonpolar. The polarization of the reagents was determined by the total dipole moment of the solvent molecule.

The molar ratio of the components of the system benzene-nitrobenzene was taken as equal to 2:5, in accordance with the solvate $2C_6H_6 \cdot 5C_6H_5NO_2$ found in the previous work [1].

The formation of a nitrobenzene solvate of benzene is a reversible process. The nitrobenzene reaction changes only the electron system of the benzene ring. In thisnitrobenzene differs from such strongly polarizing solvents as, for example, sulfuric acid, where solution is accompanied by irreversible sulfonation [7].

The idea that the initiator of the reaction adds to the reagent molecule is in agreement with the experimental data on the effect of the nature of the catalyst on the orientation of the substituent in the benzene ring [3, 8].

EXPERIMENTAL

The reagents were synthesized and purified in the usual way [1]. Their optical purity was checked by the ultraviolet absorption spectra, which were determined with an ISP-22 spectrograph.

The bromination reactions were carried out in a round-bottomed flask with a reflux condenser by boiling gently on a water bath for 4 hours. Then the reaction mixture was washed with aqueous alkali and water, dried with fused calcium chloride and put through fractional distillation. The fractions collected at 140–200° were distilled again; bromobenzene was taken off in the range 152–153°. After washing with sulfuric acid and water, drying with calcium chloride and distilling, the ultraviolet absorption spectrum was determined for identification. Its absorption curve (Fig. 1) was identical with the absorption spectrum curve of standard, optically pure bromobenzene.* The bromobenzene was spectrographed as a liquid in isooctane solution at concentrations of

*Spectrum determined by N. A. Obraztsova.

$2.2 \cdot 10^{-1}$, $2 \cdot 10^{-2}$, and $2 \cdot 10^{-3}$ M. The available literature data is incomplete and out of date [9, 10].

The kinetics of the reaction were investigated by iodometric titration of samples of the reaction mixture, taken every 20 minutes of the reaction.

In each experiment we used 30 g of benzene (0.36 mole) and 48 g of bromine (0.30 mole). The same volume of solvent was taken namely, 92 ml (i. e., 0.90 mole of nitrobenzene, 0.97 mole of carbon tetrachloride and 0.88 mole of bromobenzene).

In the nitrobenzene solution, the bromine reacted quickly. The curve of the change in the amount of bromine was a hyperbola (Fig. 2, curve 1). After 90 minutes 11 g of bromine had been consumed in bromination. The yield of bromobenze was 33.1%. Dibromobenzene was not formed.

Benzene, dissolved in carbon tetrachloride, did not react with bromine under the same conditions of concentration, temperature and time of reaction (Fig. 2, curve 2). The amount of bromine remained almost constant over 240 minutes.

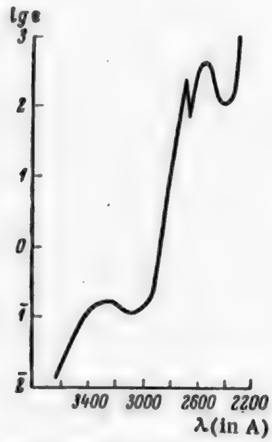

Fig. 1. Ultraviolet absorption of bromobenzene in isooctane solution.

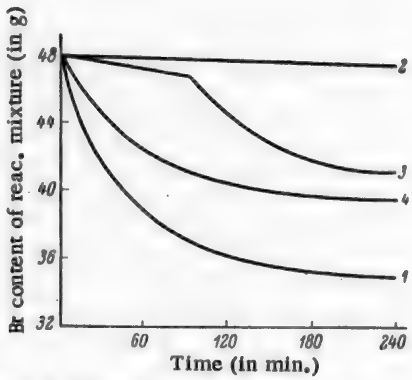

Fig. 2. Bromination of benzene 1) in nitrobenzene solution, 2) in carbontetrachloride solution, 3) in the absence of a solvent, 4) in bromobenzene solution.

In the absence of solvent, the bromination reaction maintained itself by thermal excitation (Fig. 2, curve 3). The thermal excitation corresponded to the linear part of the curve. After 90 minutes, 2 g of bromine had been consumed in the reaction. The bromobenzene, accumulating after 90 minutes began to act as a polar solvent and initiated bromination similar to nitrobenzene, only more weakly. This corresponds to the hyperbolic part of the curve. The yield of bromobenzene was 10.3%.

The initiating effect of bromobenzene as a polar solvent in the bomination of benzene was shown by the fact that the kinetic curve of the reaction of bromine in bromobenzene solution (Fig. 2, curve 4) was exactly like the curve for nitrobenzene solution. After 90 minutes, 6 g of bromine had been consumed in the reaction. The yield of bromobenzene, determined by the increase in the amount of it at the end of the reaction, was 15.3%. Dibromobenzene was not formed.

SUMMARY

1. The bromination of benzene was investigated in solvents — nitrobenzene, bromobenzene, carbon tetrachloride — and without solvents.

2. The solvating nitrobenzene medium which decreases the activation energy is the most favorable for the bromination of benzene.

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BORON FLUORIDE AS A CATALYST IN ORGANIC CHEMISTRY

XIII. ALKYLATION OF 2- AND 4-BROMOPHENOLS BY PSEUDOBUTYLENE AND CYCLOHEXENE IN THE PRESENCE OF THE CATALYSTS $BF_3 \cdot H_3PO_4$ and $BF_3 \cdot O(C_2H_5)_2$

S. V. Zabgorodny and V. G. Kryuchkova

Although halophenols possess high reactivity and are relatively accessible materials, while alkylhalophenols and their alkyl ethers have a definite practical value, the alkylation of halophenols with olefins has been studied veryl little. We decided to investigate the alkylation of halophenols with olefins and cycloolefins in the presence of catalysts based on boron fluoride.

The alkylation of 2- and 4-chlorophenols with 2-butene [1], 2-pentene [2] and cyclohexene [3] in the presence of the ethyl etherate of boron fluoride was described in previous papers. The alkylation of 2- and 4-bromophenols by pseudobutylene and cyclohexene in the presence of the catalysts $BF_3 \cdot H_3PO_4$ and $BF_3 \cdot O(C_2H_5)_2$ was studied in the present work. It was shown that phenol products or a mixture of ether and phenol products (depending on the conditions) were formed by the alkylation of 2-bromophenol with pseudobutylene; in all other cases, only an ether-like compound was obtained. The effect of the molar ratio of reagents and catalyst, time and temperatures of the total yield of ether and phenol compounds is shown in the table.

EXPERIMENTAL

Cyclohexene was prepared by dehydrating cyclohexanol [4] (b.p. 83–84°, d_4^{20} 0.8109, n_D^{20} 1.4450). Pseudobutylene was isolated from the pseudobutylene–divinyl fraction from the polymerization of divinyl with metallic sodium. 2-Bromophenol was the commercial preparation (d_4^{20} 1.6228 n_D^{20} 1.5860). 4-Bromophenol was prepared by the bromination of phenol [4]. The catalysts $BF_3 \cdot H_3PO_4$ and $BF_3 \cdot O(C_2H_5)_2$ were prepared by saturating a hydrous orthophosphoric acid and the absolute ethyl ether with boron fluoride.

1. Alkylation of 2-bromophenol with pseudobutylene in the presence of $BF_3 \cdot H_3PO_4$ and $BF_3 \cdot O(C_2H_5)_2$. Into a three-necked flask fitted with a mechanical stirrer, a thermometer and a gas inlet, was placed 16.65 g of 2-bromophenol and 3.11 g of $BF_3 \cdot H_3PO_4$. Pseudobutylene was introduced in the vigorously stirred mixture at such a rate that the reaction temperature did not rise above 30–32°. After introducing 10.84 g of pseudobutylene over a period of 5 hours, the reaction mixture was stirred for a further 2 hours and then as a homogeneous, light yellow liquid, it was treated with a 10% solution of NaOH until all the phenol compounds had been separated. The ether compounds, which were insoluble in alkali, were isolated, washed with water, dried with sodium sulfate and distilled. As a result, we isolated: sec-butyl ether of 2-bromophenol 2.66 g (12.06%) and sec-butyl ether of sec-butyl-2-bromophenol 4.60 g (20.86%). On treatment in the usual way with dilute hydrochloric acid and distillation, the alkaline solution yielded 7.90 g (35.83%) of sec-butyl-2-bromophenol. The data of the different experiments are summarized in the table.

Sec-butyl-2-bromophenol was a colorless liquid with a phenolic odor:

b.p. 107–110° at 6 mm, d_4^{20} 1.3400, n_D^{20} 1.5486, MR_D 54.26; calc. 54.06.
Found %: Br 34.89. M 227.7, 226.3. $C_{10}H_{13}OBr$. Calculated %: Br 34.88. M 229.

The sec-butyl ether of 2-bromophenol was a colorless liquid with a pleasant odor:

Alkylation of 2- and 4-Bromophenols With Pseudobutylene and Cyclohexene in the Presence of $BF_3 \cdot H_3PO_4$ and $BF_3 \cdot C(C_2H_5)_2$.

Experiment number	Olefin	Catalyst	Molar ratios of bromophenol, olefin and catalyst	Reaction temperature	Time (in hours)	Yield of alkylation products (in %)**		
						$C_6H_4(Br)(OR)$	$R{-}C_6H_3(Br)(OR)$	$R{-}C_6H_3(Br)(OH)$
1	Pseudobutylene	$BF_3 \cdot H_3PO_4$	0.5 : 1 : 0.10	30—32°	7	12.1	20.9	35.8
2	"	$BF_3 \cdot H_3PO_4$	0.7 : 1 : 0.10	30—32	5.5	7.8	23.9	27.0
3	"	$BF_3 \cdot H_3PO_4$	1.25 : 1 : 0.25	30—32	3	—	—	49.7
4	"	$BF_3 \cdot O(C_2H_5)_2$	1 : 1 : 0.20	18—20	10 days	44.3	—	—
5	Cyclohexene	$BF_3 \cdot H_3PO_4$	1 : 1 : 0.14	25—26	24	35.8	—	—
6	"	$BF_3 \cdot O(C_2H_5)_2$	1 : 1 : 0.14	25—26	24	37.6	—	—
7	"	$BF_3 \cdot O(C_2H_5)_2$	2 : 1 : 0.20	25—26	24	37.1	—	—
8	Pseudobutylene	$BF_3 \cdot H_3PO_4$	0.5 : 1 : 0.25	18—20	9	30.6	15.3	—
9	"	$BF_3 \cdot H_3PO_4$	1 : 1 : 0.20	18—20	12	29.1	17.4	—
10	"	$BF_3 \cdot H_3PO_4$	0.5 : 1 : 0.20	18—20	10 days	35.4	27.2	—
11	"	$BF_3 \cdot O(C_2H_5)_2$	0.5 : 1 : 0.08	18—20	10 days	39.6	5.0	—
12	Cyclohexene	$BF_3 \cdot H_3PO_4$	1 : 1 : 0.14	18—20	1	49.0	—	—
13	"	$BF^3 \cdot H_3PO_4$	1 : 1 : 0.17	18—20	3	59.2	—	—
14	"	$BF_3 \cdot H_3PO_4$	1 : 1 : 0.06	18—20	24	55.1	—	—
15	"	$BF_3 \cdot O(C_2H_5)_2$	1 : 1 : 0.18	18—20	3	57.7	—	—
16	"	$BF_3 \cdot O(C_2H_5)_2$	1 : 1 : 0.16	18—20	48	64.1	—	—
17	"	$BF_3 \cdot O(C_2H_5)_2$	2 : 1 : 0.19	18—20	3	56.7	—	—
18	"	$BF_3 \cdot O(C_2H_5)_2$	0.5 : 1 : 10	18—20	3	54.8	—	—

*Experiments 1–7 were carried out with 2-bromophenol and experiments 8–18 with 4-bromophenol.

**R — denotes the sec -butyl or cyclohexyl radical.

b.p. 86–87° at 1 mm, d_4^{20} 1.2811, n_D^{20} 1.5312, MR_D 55.31; calc. 54.19.
Found %: Br 34.42, 34. 46. M 227.7, 228.7. $C_{10}H_{13}OBr$. Calculated %: Br 34.88. M 229.

The sec-butyl ether of sec-butyl-2-bromophenol was a colorless liquid with a pleasant ether odor: :

b.p. 122–125° at 3 mm, d_4^{20} 1.2008, n_D^{20} 1-5268, MR_D72.54: calc. 72.91.
Found %: Br 28.23. $C_{14}H_{21}OBr$. Calculated %: Br 28.02.

2. Alkylation of 2-bromophenol with cyclohexene in the presence of $BF_3 \cdot H_3PO_4$ and $BF_3 \cdot O(C_2H_5)_2$. The reaction was carried out as described for pseudobutylene, but in this case the cyclohexene was added from a dropping funnel to the vigorously stirred 2-bromophenol and catalyst at such a rate that the reaction temperature did not rise above 25–26°. After adding the definite amount of cyclohexene, the reaction mixture was stirred for two hours, left for a day at room temperature and then treated in the usual way. The data of the experiments are given in the table.

The cyclohexyl ether of 2-bromophenol was a colorless liquid with a pleasant odor:

b.p. 127–128° at 1 mm, d_4^{20} 1.3214, n_D^{20} 1.5572, MR_D62.16; calc. 61.22.
Found %: Br 31.15, 31.09. M 254.0, 256.7. $C_{12}H_{15}OBr$. Calculated %: Br 31.32. M 255.2.

3. Alkylation of 4-bromophenol with pseudobutylene in the presence of $BF_3 \cdot H_3PO_4$ and $BF_3 \cdot O(C_2H_5)_2$. The reaction was carried out similarly to the alkylation of 2-bromophenol with pseudobutylene with the difference in this case that the reaction mixture was not immediately worked up after the introduction of the given amount of pseudobutylene, but was left for a definite time at room temperature. The data of the experiments are given in the table.

The sec-butyl ether of 4-bromophenol was a colorless liquid with a pleasant odor;

b.p. 95–97° at 3mm, d_4^{17} 1.2847, n_D^{20} 1.5310, MR_D 55.15; calc. 54.19.
Found %: Br 34.69. M 226.3. $C_{10}H_{13}OBr$. Calculated %: Br 34.88. M 229.0

The sec-butyl ether of 2-sec-butyl-4-bromophenol was an oily, light brown liquid:

b.p. 120–123° at 8 mm, d_4^{20} 1.2011, n_D^{20} 1.5218, MR_D 72.30: calc. 72.54.
Found %: Br 28.34. $C_{14}H_{21}OBr$. Calculated %: Br 28.04.

4. Alkylation of 4-bromophenol with cyclohexene in the presence of $BF_3 \cdot H_3PO_4$ and $BF_3 \cdot O(C_2H_5)_2$. Into a wide tube of capacity 40–50 ml was placed 17.25 g of 4-bromophenol, 2.90 g of the catalyst $BF_3 \cdot H_3PO_4$ and 8.92 g of cyclohexene. The tube was closed with a stopper, with a thermometer reaching almost to the bottom of the tube and the reaction mixture was shaken periodically for 1 hour, left at room temperature for 2 hours and treated with a 5% solution of NaOH. The reaction began immediately after mixing the reagents and catalyst and the mixture gradually acquired a dark brown color. On treating the reaction products with NaOH, the solution changed from dark brown to light yellow, from which yellowish crystals of the cyclohexyl ether of 4-bromophenol were precipitated. After recrystallization from anhydrous ethyl alcohol, the weight of these was 15.18 g of 59.23% (yield calculated on 4-bromophenol). 1.68 g of unreacted 4-bromophenol was regenerated from the alkaline solution. Data of experiments under different conditions and with the catalyst $BF_3 \cdot O(C_2H_5)_2$ are given in the table.

The cyclohexyl ether of 4-bromophenol was white crystals almost without odor: m.p. 44–45° (from anhydrous ethyl alcohol).

Found %: Br 31.17, 31.23. $C_{12}H_{15}OBr$. Calculated %: 31.32.

SUMMARY

The alkylation of 2- and 4-bromophenols with pseudobutylene and cyclohexene was studied in the presence of the catalysts $BF_3 \cdot H_3PO_4$ and $BF_3 \cdot O(C_2H_5)_2$.

The following compounds were synthesized : sec--butyl-2-bromophenol, the sec -butyl ether of 2-bromophenol, the sec -butyl ether of sec -butyl-2-bromophenol, the cyclohexyl ether of 2-bromophenol the sec - butyl ether of 4-bromophenol, the sec -butyl ether of 2-sec -butyl-4-bromophenol and the cyclohexyl ether of 4-bromophenol.

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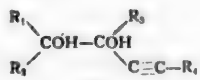
** In Russian.

INVESTIGATION OF THE REACTIONS OF PINACONES WITH SUBSTITUTED ACETYLENE RADICALS

XIV. SYNTHESIS AND REACTION OF UNSYMM. METHYL-DIPHENYL-TERTIARY-BUTYLACETYLENYL-ETHYLENE GLYCOL (1,1-DIPHENYL-2,5,5-TRIMETHYLHEXINE-3-DIOL-1,2)

E. D. Venus-Danilova, V. I. Serkova and A. V. Eltsov

The example of ditertiary acetylene α-glycols of type (1) illustrates particularly clearly the effect of the nature of the radicals and their mutual tendency towards reaction under the effect of sulfuric acid [1].



(I)

Besides the usual pinacoline reactions [2], the formation of substituted 2-hydroxydihydrofurans-2,5 or the corresponding tautomeric ethylene γ-ketoalcohols [3–5] are also characteristic of these pinacones which contain an extremely reactive acetylene bond. Quite often a mixture of acetylene ketones and substituted hydroxydihydrofurans or products of their further reaction are obtained [6–9].

With the acetylene α-glycols that we have investigated up to now, not once could we detect the products of dehydration due to the labile hydroxyl group in the α-position to the triple bond and adjacent methyl group (I; $R_3 = CH_3$).

There are indications in the literature that besides pinacoline, a dienine alcohol was also isolated as a result of the direct dehydration of trimethyl-vinylacetylenyl-ethylene glycol with $KHSO_4$ [10], while only the product from the abstraction of water was obtained from symm. dimethyl-isobutyl-acetylenyl-ethylene glycol when treated with sulfuric acid and if there was any pinacoline regrouping, it occurred only to a very slight degree [11].

It is known that phenyl-vinyl-acetylene and acetophenone are formed by heating symm. dimethyl-phenyl-phenylacetylenyl-ethylene glycol (I; $R_1 = R_3 = CH_3$; $R_2 = R_4 = C_6H_5$) with 30% sulfuric acid [12]. One can suppose from our experiments that these materials may be formed by ketonic decompostion of the enine alcohol, obtained from the original glycol by splitting out water; however we were unable to isolate this enine alcohol and elucidate its structure due to its being readily decomposed.

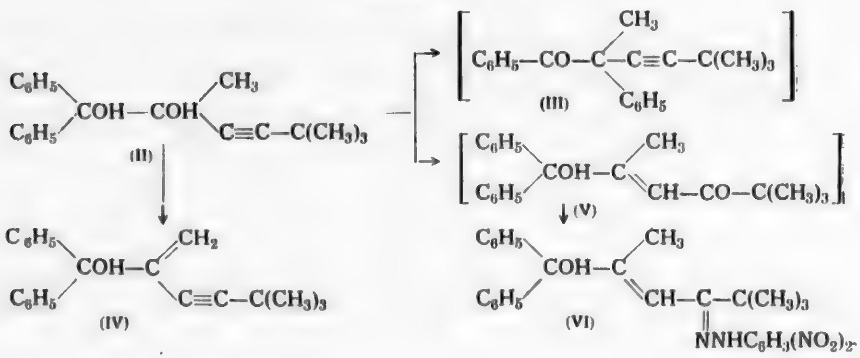
Considering this observation, as well as the data on the reaction of unsymm. methyl-diphenyl-phenylacetylenyl-ethylene glycol (I; $R_1 = R_2 = R_4 = C_6H_5$; $R_3 = CH_3$ [2], which gave only a ketone of the acetylene series in 40% yield and a large amount of tar, we thought it interesting to investigate the effect of sulfuric acid on one other pinacone of the acetylene series — unsymm. methyl-diphenyl-tertiarylbutylacetylenyl-ethylene glycol (II).

It was to be expected that, in analogy with unsymm. methyl-diphenyl-phenylacetylenyl-ethylene glycol, this pinacone would give an acetylene ketone (III), although the formation of the enine alcohol (IV) was also possible.

The experiments on the effect of sulfuric acid of varying concentrations on unsymm. methyl-diphenyl-tertiary-butylacetylenyl-ethylene glycol (II) showed that this glycol is quite stable to sulfuric acid when heated: 30% sulfuric acid did not affect it, 40% formed a mixture of the enine alcohol (IV) and the original glycol, and a single product – the enine alcohol (IV) in 85% yield with a very small amount of tar was formed only with 41.5% sulfuric acid. Neither an acetylene ketone (III), nor γ-ketoalcohol of the ethylene series (V) were thus isolated (see scheme 1).

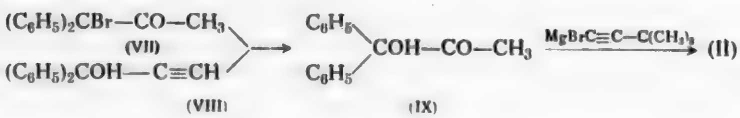
The structure of the enine alcohol – 1,1-diphenyl-2-methylen-5,5-dimethylhexin-3-ol-1 was proved by oxidizing it to obtain benzophenone and benzilic, formic and trimethylacetic acids.

Scheme 1



Unsymm. methyl-diphenyl-tertiary-butylacetylenyl-ethylene glycol (II) was synthesized as in scheme 2.

Scheme 2



The original diphenylacetylcarbinol (IX) was obtained by a method described earlier, starting with phenylacetylbromomethane (VII) [13], or, what was more convenient, using M. G. Kucherov's method, by the hydration of diphenylacetylenylcarbinol, which could be readily synthesized, in analogy with the formation of acetylenylcyclohexanol [14] from benzophenone and sodium acetylide in liquid ammonia.

We should note the unexpected reaction of 2,4-dinitrophenylhydrazine in sulfuric acid with unsymm. methyl-diphenyl-tertiary-butylacetylenyl-ethylene glycol (II), giving the 2,4-dinitrophenylhydrazone (VI) of the isomeric ethylene γ-ketoalcohol (V). The oily liquid, obtained by the action of 40% sulfuric acid on unsymm. methyl-diphenyl-tertiary-butylacetylenyl-ethylene glycol, which also contained a small amount of the latter, gave with 2,4-dinitrophenylhydrazine (in an alcohol solution with sulfuric acid) [15] a yellow precipitate, which, according to analysis for nitrogen, could be considered as the 2,4-dinitrophenylhydrazone of the acetylene ketone (III). However, the liquid product obtained by the action of 41.5% sulfuric acid on the acetylene glycol, was the pure enine alcohol (IV) and contained no traces of ketone (III) and did not react with 2,4-dinitrophenylhydrazine. It was proved that the 2,4-dinitrophenylhydrazone obtained did not correspond to the acetylene ketone (III), but to the ethylene γ-ketoalcohol (V) which could form as a result of isomerization of the acetylene glycol (II) in an acidic medium.

The same 2,4-dinitrophenylhydrazone was obtained by treating the acetylene glycol directly with 2,4-dinitrophenylhydrazine under analogous conditions. Probably, in the presence of sulfuric acid in the alcohol solution, a certain amount of the glycol was converted into the unsaturated γ-ketoalcohol (V), which reacted with

2,4-dinitrophenylhydrazine, the latter affecting the course of the reaction.

It should be noted that when the reaction of an alcohol solution of the glycol and sulfuric acid took place at ordinary temperature, no ethylene γ-ketoalcohol was detected and the glycol remained unchanged under these conditions.

The formation of 2,4-dinitrophenylhydrazones of unsaturated ketones from tertiary α-acetylene alcohols by the action of an alcohol solution of 2,4-dinitrophenylhydrazine in the presence of sulfuric acid is described in the literature [16]. We were the first to discover this reaction for ditertiary acetylene α-glycols of type (I).

EXPERIMENTAL

1. Synthesis of starting materials

Diphenylacetylenylcarbinol. Into a flask containing liquid ammonia (1 liter, d 0.817) was placed 23 g of metallic sodium and at the same time, a strong current of acetylene was passed through. An ether solution of 175 g of benzophenone was added dropwise to the sodium monacetylide obtained. After treating the mixture with water, extracting the product with ether and distilling off the solvent, we isolated 170 g (85%) of diphenyl-acetylenylcarbinol with b.p. 154° (3 mm) and m.p. 44°, which agrees with literature data [17].

Diphenylacetylcarbinol. a) 15 g of diphenylacetylenylcarbinol, 5 ml of sulfuric acid (d 1.84), 200 ml of water and 5 g of mercuric oxide were heated on a water bath for 1 hour, with vigorous stirring. On mixing, there immediately came down a white, flocculent precipitate, which quickly disappeared on heating and the reaction mixture partly became tarry. After extracting with ether, drying and distilling off the ether, the quite strongly tarry liquid was distilled in vacuum and boiled at 160° (3 mm). We obtained 3 g (19%) of a substance, which melted at 65° [13] and did not depress the melting point of authentic diphenylacetylcarbinol. Partial isomerization of the starting diphenylacetylenylcarbinol under the effect of the sulfuric acid into β,β-diphenyl-cinnamaldehyde and polymerization of the latter on heating (tar) explains, probably, the low yield of the ketoalcohol.

b) To 10 g of mercuric oxide and 400 ml of dilute sulfuric acid (1 : 25) was added a solution of 30 g of diphenylacetylenylcarbinol in 150 ml of 96% ethyl alcohol. The white, flocculent precipitate, which immediately formed, gradually disappeared on heating on a water bath (70°) without noticeable tar formation in the reaction mixture; by the usual methods we isolated 9.6 g (36%) of diphenylacetylcarbinol with m.p. 65–66°.

In four experiments we obtained 28 g (on an average 26%) of diphenylacetylcarbinol from 100 g of diphenyl-acetylenylcarbinol.

In a synthesis of diphenylacetylcarbinol by the hydrolysis of diphenylacetylbromomethane [13], we synthesized 30 g (56%) of diphenylacetylcarbinol with m.p. 65–66°.

2. Synthesis of unsymm. methyl-diphenyl-tertiarylbutylacetylenyl-ethylene glycol (1,1-diphenyl-2,5,5-trimethylhexine-3-diol-1,2)

To tertiary butylacetylenylmagnesium bromide, prepared from 4.8 g of magnesium, 22 g of ethyl bromide and 17 g of tertiary butylacetylene, was added an ether solution of 22.6 g of diphenyl-acetylcarbinol. The complex obtained was decomposed with dilute sulfuric acid and the ether extract was washed with a dilute solution of soda and dried with sodium sulfate. After distilling off the ether, the thick oily substance quickly crystallized and after recrystallization from petroleum ether, melted at 106–107°.

The substance obtained reacted with methylmagnesium iodide decolorized an aqueous solution of potassium permanganate and a solution of bromine in chloroform and did not react with semicarbazide acetate. On heating with potash [18] at 220°, it decomposed with the liberation of tertiary-butylacetylene.

According to analytical data, this substance was an acetylene α-glycol – 1,1-diphenyl-2,5,5-trimethyl-hexine-3-diol-1,2 (unsymm. methyl-diphenyl-tertiary butylacetylenyl-ethylene glycol).

Found %: C 81.57, 81.51; H 8.00, 7.67; OH 11.50. M 300. $C_{21}H_{24}O_2$. Calculated %: C 81.81; H 7.79; OH 11.03. M 308.

In four syntheses we obtained 50 g (60%) of the acetylene glycol.

The action of 2,4-dinitrophenylhydrazine on unsymm. methyl-diphenyl-tertiary-butylacetylenyl-ethylene glycol. The reaction of the glycol with 2,4-dinitrophenylhydrazine in alcohol solution in the presence of sulfuric acid, was carried out under the usual conditions [15]. After 6–8 hours a yellow precipitate formed, which melted at 177–178°, after recrystallization from a mixture of alcohol and ethyl acetate, and, according to analysis data, was the 2,4-dinitrophenylhydrazone of the ethylene α-ketoalcohol– 1,1-diphenyl-2,5,5-trimethylhexen-2-ol-1-one-4(V).

Found %: C 66.31; H 5.61; N 11.74. $C_{27}H_{28}O_5N_4$. Calculated %: C 66.39; H 5.74; N 11.48.

3. The action of sulfuric acid in various concentrations on unsymm. methyl-diphenyl-tertiary-butylacetylenyl-ethylene glycol

On treating an alcohol solution of the glycol at normal temperature with an alcohol-water solution of sulfuric acid (corresponding to the preparation of 2,4-dinitrophenylhydrazones), no reaction was observed in a period of more than 2 weeks.

On heating the glycol with 30% aqueous sulfuric acid for 2 hours while the mixture boiled gently, the unreacted glycol was also recovered.

Heating for 2 hours at 110–130° with 45% sulfuric acid produced a great deal of tar in the reaction mixture so that it was impossible to isolate individual reaction products.

The action of 40% sulfuric acid on the glycol. 7 g of the glycol was heated with 70 ml of 40% sulfuric acid for 3 hours while the reaction mixture boiled gently. The mixture of solid and oily products was isolated by the usual method. After purifying on a porous plate and washing with petroleum ether, the solid substance melted at 107° and corresponded to the starting acetylenic glycol (mixed melting point).

The liquid gave a positive reaction for a hydroxyl group and did not react with semicarbazide acetate, but on standing with an alcohol solution of 2,4-dinitrophenylhydrazine sulfate [15], gave a yellow precipitate, which melted at 177–178° after recrystallization from a mixture of alcohol and ethyl acetate.

This did not depress the melting point of the 2,4-dinitrophenylhydrazone, obtained by treating the acetylene glycol with 2,4-dinitrophenylhydrazine.

Found %: C 66.22; H 5.68; N 11.70. $C_{27}H_{28}O_5N_4$ (hydrazone of the ethylene γ-ketoalcohol VI). Calculated %: C 66.39; H 5.74; N 11.48. $C_{27}H_{26}O_4N_4$ (hydrazone of the acetylene ketone III). Calculated %: C 68.93; H 5.53; N 11.91.

Consequently, the hydrazone obtained was a derivative of the ethylene γ-ketoalcohol, formed from the starting glycol, which was mixed with the liquid reaction product.

Owing to the small amount of the liquid reaction product, it was not purified from the glycol present and was not examined in this experiment.

The action of 41.5% sulfuric acid on the glycol. 10 g of the glycol and 10 times the amount of 41.5% sulfuric acid were heated and stirred for 2.5 hours, while boiling gently. The light yellow liquid isolated reacted with methylmagnesium iodide and immediately decolorized a chloroform solution of bromine and an aqueous solution of potassium permanganate. Reactions with 2,4-dinitrophenylhydrazine and semicarbazide were negative.

Distillation in vacuum gave two fractions: 1st b.p. 159–160° (2 mm), 5 g; 2nd b.p. 160–165° (2 mm), 3 g; in the residue was a small amount of tarry material.

According to analytical data the first fraction was an enine alcohol – 1,1-diphenyl-2-methylen-5,5-dimethylhexin-3-ol-1 (IV), formed as a result of splitting out water from the acetylene α-glycol (II).

B.p. 159–160° (2 mm), d_4^{20} 1.0550, n_D^{20} 1.5660, MR_D 89.90. $C_{21}H_{22}O$F F. calc. 91.03; MR_D 1.13.
Found %: C 86.97, 87.15; H 7.63, 7.88; OH 6.01. M 273. $C_{21}H_{22}O$. Calculated %: C 86.89; H 7.58; OH 5.80. M 290.

To confirm the proposed structure, the enine alcohol was oxidized with potassium permanganate in a water-pyridine solution. We used 3 g of alcohol and 7 g of potassium permanganate (5 g as a 2% aqueous solution and 2 g in a dry, finely powdered state). On adding 50 ml of pyridine, the oxidation was noticeably speeded up. After separating off the manganese dioxide and distilling off the pyridine in vacuum, the acid and neutral oxidation products were separated by the usual method. In the neutral products we found only benzophenone, which was characterized by its melting point and the preparation of a semicarbazone and a 2,4-dinitrophenylhydrazone (mixed melting points).

On decomposing the salts of the organic acids with dilute sulfuric acid, a copious precipitate formed, which partly sublimed. The sublimed material melted at 120–121° and was benzoic acid (mixed melting point). The benzoic acid was extracted from the precipitate with petroleum ether. The insoluble part gave a red color with concentrated sulfuric acid, melted at 150° and did not depress the melting point of authentic benzilic acid [19]. On heating the aqueous solution of the acids to boiling, there distilled off 3–4 ml of a liquid, in which was detected formic acid by the characteristic reactions with mercuric chloride and an ammoniacal solution of silver oxide. After extraction with ether, the residual aqueous solution of the acids gave a low melting mass with a sharply acid reaction. The equivalent of the acid was determined and we also prepared its silver salt through the ammonium one.

Found equiv. 97.7. $C_5H_{10}O_2$. Calculated equiv. 102.
Found %: Ag 52.00, 52.04. $C_5H_9O_2Ag$. Calculated %: Ag 51.67.

According to the analytical data, the acid obtained corresponded to trimethylacetic.

On oxidizing the product with b.p. 159–160° (2 mm), we obtained benzophenone and benzoic, formic and trimethylacetic acids, which confirmed that the product was 1,1-diphenyl-2-methylen-5,5-dimethylhexin-3--ol-1.

The second fraction with b.p. 160–165° (2 mm), obtained on distilling the product of treating the acetylene glycol with 41.5% sulfuric acid, gave the same qualitative reactions and had constants close to the 1st fraction (n_D^{20} 1.5669).

Found %: OH 4.80. M 242. $C_{21}H_{22}O$. Calculated %: OH 5.80. M 290.

Consequently, here also we had the enine alcohol, but slightly impure.

In all we obtained 8 g (85%) of the enine alcohol by splitting out water from the acetylene α-glycol.

SUMMARY

1. A new example of a pinacone of the acetylene series was synthesized – unsymm. methyl-diphenyl-tertiary-butylacetylenyl-ethylene glycol (1,1-diphenyl-2,5,5-trimethylhexine-3-diol-1,2) and it was shown that this pinacone, in contrast to those studied earlier, was converted into an enine alcohol – 1,1-diphenyl-2-methylen--5,5-dimethylhexin-3-ol-1 – by heating with a 41.5% aqueous solution of sulfuric acid.

2. It was found that the reaction of an alcohol solution of unsymm. methyl-diphenyl-tertiary-butylacetylenyl-ethylene glycol with 2,4-dinitrophenylhydrazine in the presence of sulfuric acid gave a 2,4-dinitrophenylhydrazone, which corresponded to the isomeric ethylene γ-ketoalcohol – 1,1-diphenyl-2,5,5-trimethylhexine-2--ol-1-one-4.

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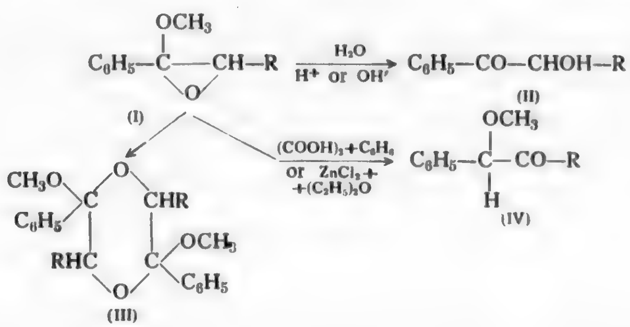
INVESTIGATION IN THE FIELD OF CYCLIC ACETALS OF HYDROXYCARBONYL COMPOUNDS

VIII. THE METHYL LACTOLIDE OF PROPYLBENZOYLCARBINOL AND ITS REACTIONS

T. I. Temnikova and V. A. Ivanova

Methyl lactolides of α-ketoalcohols which are at the same time α-methoxy-α-oxides (I), react in the presence of acid reagents in different ways depending on the acid's strength and on the character of the solvent used; α-ketoalcohols or their derivatives are thus formed. In all cases, the oxide ring is opened, but the final reaction product depends on the activity of the solvent — whether it enters into the reaction or whether the process is accomplished without its participation, as well as on the stability of the first reaction product formed. Thus, for example, in all cases α-ketoalcohols, corresponding to the methyl lactolide taken, are formed by the action of aqueous acid solutions [1, 2]. Reaction with methyl alcohol in the presence of HCl gives compounds which contain a dioxane ring — cyclodimethyl dilactolides (III) [1, 2, 5]. Isomerization of the methyl lactolide occurs if the solvent is incapable of reacting with methyl lactolides in the presence of catalysts, affecting the oxide ring [3, 4, 8].



The purpose of this work was to study the reaction of methyl lactolides of α-ketoalcohols when treated with acid reagents in the presence of carbonyl-containing materials and, in particular, in acetone solution. It seemed interesting to find out whether the carbonyl-containing compound would add to the oxide ring under these conditions or whether the methyl lactolide reaction would proceed the same as in the presence of solvents that are inactive with respect to addition reactions at the oxide ring. The investigations were carried out using as the example, the methyl lactolide of propylbenzoylcarbinol which was first obtained by us using the usual method of synthesis — by the action of sodium methylate on α-bromobutyl phenyl ketone. The formation of this substance and the investigation of its reactions were in themselves of interest as at present only three methyl lactolides of ketoalcohols of the aliphatic-aromatic series have been described in the literature. The methyl lactolide has a typical spectrum in the infrared region with strong absorption at 917 cm^{-1} [8].

The action of sulfuric acid on the methyl lactolide (I) ($R = n.\text{-}C_3H_7$) in an acetone solution both in the cold

and when heated, as well as under different working conditions, gave only two reaction products: the cyclodimethyl dilactolide of propylbenzoylcarbinol (III) (R = n.-C_3H_7) and the ketoalcohol, n.-propylbenzoylcarbinol (II) (R = n.-C_3H_7). The cyclodimethyl dilactolide of propylbenzoylcarbinol, which has not been described in the literature, was prepared for comparison and identification also by the usual method — by the action of 1% HCl in methyl alcohol on the methyl lactolide [1, 2]. The formation of the ketoalcohol was explained by the hydrolysis of the methyl lactolide with water, which we were unable to remove from the acetone by the usual drying method; the water content of the acetone was determined by the carbide method and equalled 0.2%. A very small amount of a material, containing a methoxyl group, was among the liquid reaction products besides the ketoalcohol, but it could not be isolated in a pure state; apparently, isomerization of the methyl lactolide into the methyl ether of the isomeric ketoalcohol occurred at the same time to a very slight degree in the acidic medium. Practically complete isomerization of this type occurred when the methyl lactolide was treated with an $SnCl_4$ solution in carbon tetrachloride or zinc chloride in ether. The ether of the ketoalcohol (IV) (R = n.-C_3H_7), obtained has an absorption maximum in the infrared spectrum at 1718 cm^{-1}, typical of a carbonyl not conjugated with a phenyl group [8]. An attempt to react benzophenone in a CCl_4 solution with the methyl lactolide in the presence of $SnCl_4$ was unsuccessful; the benzophenone was recovered in full and only the methyl ether of the ketoalcohol was obtained in the distillation.

Thus, the carbonyl containing material could not be reacted with the methyl lactolide of the aliphatic-aromatic ketoalcohol; under the conditions used only the usual reaction products of the methyl lactolide were obtained. This should be noted as α-oxides react relatively readily in the presence of acids or $SnCl_4$ with acetone, giving the corresponding 1,3-dioxolanes [6, 7].

EXPERIMENTAL

Preparation of the methyl lactolide of propylbenzoylcarbinol (I) (R = n.-C_3H_7). An ether solution of 22 g of α-bromobutyl phenyl ketone (b.p. 130–133° at 4 mm) was added dropwise to a suspension of metallic sodium in absolute ether with vigorous stirring. It was worked up in the usual way [1, 2]. We obtained 9.9 g (56%) of the methyl lactolide. It was a colorless liquid with a pleasant smell.

B.p. 94–96° at 4 mm, d_4^{20} 1.0239, n_D^{20} 1.4940, MR_D 55.00; calc. 56.44.
Found %: C 75.13, 75.20; H 8.42, 8.57; OCH_3 16.4. $C_{12}H_{16}O_2$. Calculated %: C 75.00; H 8.33; OCH_3 16.1.

Conversion of the methyl lactolide of propylbenzoylcarbinol by H_2SO_4 in acetone. With vigorous stirring and cooling, 1 drop of concentrated H_2SO_4 was added to 20 ml of acetone containing 0.2% moisture; then a solution of 5 g of the methyl lactolide in 5 g of acetone was added slowly, dropwise to the boiling solution, after which boiling was continued for a further 5 minutes. On adding the methyl lactolide, colorless crystals began to separate and after cooling they were separated off and recrystallized from benzene. The yield was 0.62 g. The m.p. was 243–245°.

Found %: C 75.3, 75.14; H 8.5, 8.62; OCH_3 16.07. M 393. $C_{24}H_{32}O_4$. Calculated %: C 75.00; H 8.33; OCH_3 16.1. M 384.

According to analytical data this was the cyclodimethyl dilactolide of propylbenzoylcarbinol (III) (R = n.-C_3H_7). The same cyclodimethyl dilactolide was prepared from the methyl lactolide of propylbenzoylcarbinol by treatment with 1.5% HCl in methyl alcohol.

The acetone solution remaining after filtering off the crystals was freed from sulfuric acid with fused potash and was distilled, first at normal pressure and then in vacuum. The main mass distilled over 129–130° (7 mm), n_D^{20} 1.5180. The substance contained practically no -OCH_3 groups and apparently was the almost pure α-ketoalcohol, propylbenzoylcarbinol (act. H 0.9).

Found %: C 74.60, 74.39; H 846, 8.01. $C_{11}H_{14}O_2$. Calculated %: C 74.15; H 8.31.

2,4-Dinitrophenylhydrazone — m.p. 98–100°.

Found %: N 15.49, 15.60. $C_{17}H_{18}O_5N_4$. Calculated %: N 15.64.

Isomerization of the methyl lactolide of propylbenzoylcarbinol into the methyl ether of phenylpropylcarbinol in the presence of $SnCl_4$. a) 3 g of the methyl lactolide of propylbenzoylcarbinol was added dropwise to a solution of 0.12 g of anhydrous $SnCl_4$ in 23 ml of CCl_4. The reaction mixture was stirred for 1 hour, then a 17% aqueous solution of KOH was added to the solution, the aqueous solution was separated and the CCl_4 solution was dried with potash. Next day, after distilling off the CCl_4, the residue was distilled in vacuum to yield a substance with b.p. 117–120° at 6 mm.

d_4^{20} 1.0608, n_D^{20} 1.5198, MR_D 55.00; calc. 55.67.
Found %: C 74.95; H 8.13; OCH_3 16.5. $C_{12}H_{16}O_2$. Calculated %: C 75.00; H 8;33; OCH_3 16.1.

The methoxyketone was characterized by the 2,4-dinitrophenylhydrazone. The m.p. was 103–104°.

Found %: N 14.88, 14.85. $C_{18}H_{20}O_5N_4$. Calculated %: N 15.05.

SUMMARY

The methyl lactolide of propylbenzoylcarbinol — the oxide of α-methoxy-α-phenyl-β-propylethylene — was prepared and characterized. The methyl lactolide is readily dimerized into a dioxane derivative and hydrolyzes to the ketoalcohol — propylbenzoylcarbinol.

The methyl lactolide undergoes isomerization into the methyl ether of phenylpropylcarbinol when treated with anhydrous $SnCl_4$.

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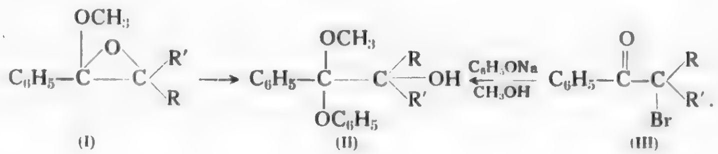
*T. p. = C. B. Translation pagination.

PREPARATION OF METHYL PHENYL KETALS OF ALIPHATIC–AROMATIC α-KETOALCOHOLS

G. A. Ugolnikova

In the last few years, much attention has been paid to the chemistry of various compounds containing a phenoxy group as they may be used as chemical weed killers and plant growth stimulants [1], as well as fungicides [2]; α-phenoxyamine compounds, readily obtained from α-phenoxyketones, are of pharmacological interest [3]. Due to this we continued the work, begun earlier [4] on the preparation of methyl phenyl ketals of aliphatic-aromatic α-ketoalcohols. The first example of such a type of α-ketoalcohol derivative was obtained in this work by the action of phenol on the methyl lactolide of methylbenzoylcarbinol (I) ($R = CH_3$; $R' = H$); here, as well as in treatment with other acidic reagents [5], the opening of the oxide ring from the methoxy group side was observed and the methyl phenyl ketal of methylbenzoylcarbinol (II) ($R = CH_3$; $R' = H$) was formed.



The methyl phenyl ketal was also obtained by the action of sodium phenate on α-bromoethyl phenyl ketone (III) ($R = CH_3$; $R' = H$) in a methyl alcohol solution. As usual, α-phenoxyethyl phenyl ketone was obtained by the action of sodium phenate on the bromoketone in other solvents (ether, acetone). In connection with this, it is interesting to note that the reaction proceeded differently when potassium 2,4-dichlorophenate in a methyl alcohol solution was treated with α-bromoacetone and 2,4-dichlorophenoxyacetone was obtained, as in other solvents [6].

It seemed interesting to find out whether the formation of mixed ketals would occur in the action of phenol on the methyl lactolides of other aliphatic-aromatic α-ketoalcohols homologs of methylbenzoylcarbinol, as well as in the action of sodium phenate in a methyl alcohol solution on their corresponding α-bromoketones.

The reaction of the methyl lactolides of three aliphatic aromatic ketoalcohols – ethylbenzoylcarbinol ($R = C_2H_5$; $R' = H$), propylbenzoylcarbinol ($R = C_3H_7$; $R' = H$) and dimethylbenzoylcarbinol ($R = R' = CH_3$) – with phenol were studied in this paper. In all cases, methyl phenyl ketals (II), corresponding to these ketoalcohols, were obtained. These same ketals were obtained by the action of sodium phenate in methyl alcohol solution on the α-bromoketones corresponding to the above ketoalcohols. Methyl phenyl ketals are readily hydrolyzed by heating to 40° with a 5% aqueous-alcohol solution of H_2SO_4 with the formation of methyl alcohol, phenol and α-ketoalcohols corresponding to them.

EXPERIMENTAL

1. Preparation of 1-methoxy-1-phenoxy-1-phenyl-2-methyl-propanol-2 (methylphenyl ketal of dimethylbenzoyl carbinol). a) The reaction of the methyl lactolide of dimethylbenzoylcarbinol with phenol. A solution of 5 g of phenol in 60 ml of benzene was added to 8 g of methyl lactolide [4]. The mixture was left for a day at room temperature. The benzene was distilled off in vacuum and the residual crystals were recrystallized from methyl alcohol when they had m.p. 121.5–122°.

b) The reaction of α-bromoisopropyl phenyl ketone with sodium phenate. A solution of 10 g of the bromoketone in 10 ml of methanol was added to a solution of sodium phenate (1.01 g of sodium, 4.14 g of phenol and 30 ml of methanol). The solution became slightly yellow. The reaction mixture was stirred and heated at 40–50° until it gave a negative Beilstein test for halogen. The precipitate of NaBr was filtered and washed with methanol. After evaporating off the methanol in vacuum, crystals remained, which melted at 121–122° after 2 recrystallizations from methanol. A mixed melting point with the crystals obtained from the oxide was not depressed.

Found %: C 74.96; H 7.75; OCH_3 11.61; act. H 0.8. M 270.4. $C_{17}H_{20}O_3$. Calculated %: C 75.00; H 7.37; OCH_3 11.40; act. H 1.0. M 272.

Hydrolysis of the ketal. 2 g of the substance was dissolved by shaking and heating to 40° in a mixture of 30 ml of ethanol and 11.5 ml of 5% H_2SO_4. After solution, the alcohol was distilled off and the hydrolysis product twice extracted with ether. The ether extract was twice washed with 5% NaOH and dried over baked Na_2SO_4. The ether was distilled off and by the usual method a semicarbazone was prepared from the residual oil (m.p. 181°, a mixed m.p. with the semicarbazone of authentic dimethylbenzoylcarbinol was not depressed). The alkaline solution was acidified with 5% H_2SO_4 and steam distilled. The presence of phenol in the distillate was proved by the color with ferric chloride and the preparation of triiodophenol (m.p. 158°).

2. Preparation of 1-methoxy-1-phenoxy-1-phenylbutanol-2 (methyl phenyl ketal of ethylbenzoylcarbinol). a) The reaction of the methyl lactolide of ethylbenzoylcarbinol with phenol. 1.11 g of the methyl lactolide was added to a solution of 0.53 g of phenol in 6 ml of benzene. The mixture was left for a day at room temperature. Next day, large crystals (m.p. 138–140°) had formed, which melted at 143° after recrystallization from methanol.

b) The reaction of α-bromopropyl phenyl ketone with sodium phenate. The reaction was carried out as in Experiment 1. We used 15 g of the bromoketone, 6.21 g of phenol, 1.68 g of sodium and 60 ml of methanol. The large crystals formed were washed with water to remove sodium bromide and melted at 143° after recrystallization from methanol. A mixed melting point with the crystals obtained from the oxide was not depressed.

Found %: C 75.17, 75.13; H 7.40, 7.42; OCH_3 11.69; act. H 0.986. M 271.7. $C_{17}H_{20}O_3$. Calculated %: C 75.00; H 7.37; OCH_3 11.39; act. H 1.0. M 272.

Hydrolysis of the ketal. The hydrolysis was carried out as in Experiment 1. The ketoalcohol obtained reduced Fehling's solution. It was treated with a 2% solution of HCl in methanol. The white needle-like crystals formed melted at 239° [8] after recrystallization from benzene. The phenol in the aqueous extract was characterized as triiodophenol.

3. Preparation of 1-methoxy-1-phenoxy-1-phenylpentanol-2 (methyl phenyl ketal of propylbenzoylcarbinol). a) The reaction of the methyl lactolide of propylbenzoylcarbinol with phenol. 1.19 g of phenol was dissolved in 20 ml of benzene and added to 2.43 g of oxide [7]. After 3 days the solution took on a gelatinous form and began to crystallize slowly. The crystals were filtered off and after recrystallization from methanol, melted at 109.5–110°.

b) The reaction of α-bromo-n-butyl phenyl ketone with sodium phenate. The reaction was carried out as in Experiments 1 and 2, and we used 10 g of the bromoketone, 3.89 g of phenol, 0.955 g of sodium and 30 ml of methanol. The sodium bromide formed was filtered off, the methanol distilled off from the solution and the gelatinous mass formed quickly crystallized. The crystals melted at 110° after recrystallization from methanol and a mixed melting point with the crystals from the oxide was not depressed.

Found %: C 75.28, 75.45; H 8.00, 7.97; OCH_3 7.93; act. H 0.96. M 285.2. $C_{18}H_{22}O_3$. Calculated % C 75.48; H 7.74; OCH_3 8.03; act. H 1.00. M 286.

Hydrolysis of the ketal. The hydrolysis was carried out as in Experiment 1. The ketoalcohol obtained was characterized as the osazone [7], m.p. 236–237°.

Found %: N 20.88, 20.92. $C_{23}H_{20}O_8N_8$. Calculated %: N 20.89.

The phenol in the aqueous extract was characterized as triiodophenol.

In conclusion I would like to thank T. I. Temnikova for suggesting the subject and constant help in the work.

SUMMARY

The action of phenol on the methyl lactolides of aliphatic-aromatic α-ketoalcohols, regardless of the length and branching of the aliphatic chain, results in the opening of the oxide ring from the methoxy group side and the formation of methyl phenyl ketals corresponding to the α-ketoalcohol. The same ketals are formed by the action of sodium phenate in methyl alcohol solution on the bromoketones corresponding to the α-ketoalcohol. Methyl phenyl ketals are readily hydrolyzed when heated gently with a 5% aqueous-alcohol solution of sulfuric acid.

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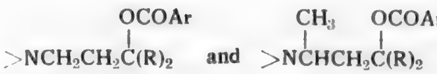
SYNTHETIC ANESTHETICS

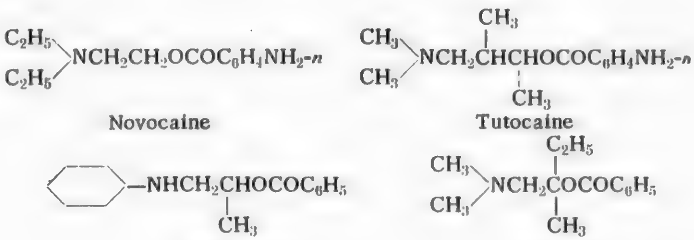
XII. ESTERS OF TERTIARY γ-DIALKYLAMINOPROPANOLS AND γ-DIALKYLAMINOBUTANOLS

I. N. Nazarov and R. I. Kruglikova

In searching for new anesthetics, we synthesized a series of esters of tertiary γ-dialkylaminopropanols and γ-dialkylaminobutanols of the type

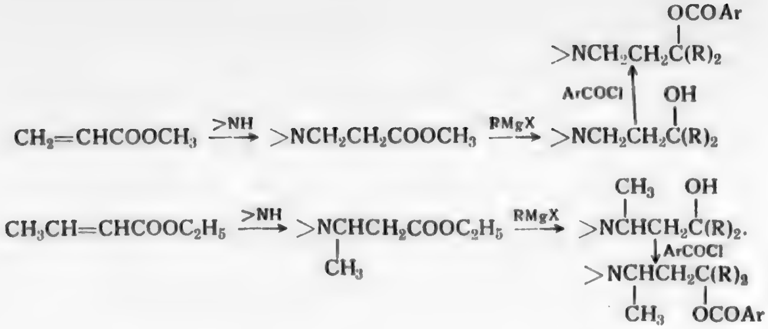


While the esters of primary amino alcohols (novocaine analogs) have been investigated very thoroughly and the esters of secondary amino alcohols (tutocaine, hexylcaine, etc.) in some detail, only some analogs similar to stovaine have been investigated in the series of esters of tertiary amino alcohols [1].

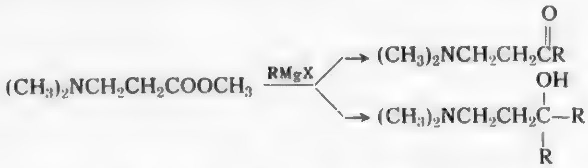


Novocaine Tutocaine Hexylcaine Stovaine

It seems likely from the data available that an increase in the carbon chain between the nitrogen and oxygen (amino alcohol chain) usually results in an increase in physiological activity and toxicity of the compound, and furthermore, the activity increases more rapidly in certain cases. Thus, for example, the anesthetic effect of p-aminobenzoates of γ-diethylamino- and γ-dibutylaminopropanols is greater than that of novacaine. It seemed interesting to investigate the physiological activity of esters of tertiary amino alcohols and to establish its relation to the structure of the compounds in this series (the character of the radicals at the tertiary carbon atom, the character of the amino group, the presence of a substituent in the amino alcohol chain). For this purpose, we synthesized tertiary amino alcohols (I–IX) and their corresponding esters (XIV–XXV). The tertiary γ-dialkylamino alcohols were obtained by the action of Grignard reagents on β-dialkylaminopropionic and β-dialkylaminobutyric esters, which in their turn were obtained in good yields by the addition of secondary amines to methyl acrylate and ethyl crotonate.



In carrying out the Grignard reaction with methyl-β-dimethylaminopropionate, it was noticed that as the radical of the organo-magnesium compound increased in size, the yield of tertiary amino alcohol decreased and the yield of the intermediary reaction product — the amino ketone — increased.



R		CH_3	C_2H_5	C_3H_7	C_4H_9	iso-C_5H_{11}
Alcohol yield	%	55	35	26	21.5	9.6
Ketone yield	%	0	21.3	26	35.5	61

The Grignard reaction usually stops at the ketone formation stage only when the organo-magnesium compound contains a heavy or branching radical [2]. An analogous phenomenon was also observed by other investigators [3] in the formation of a mixture of alcohol and ketone or even only ketone by the Grignard reaction in the presence of a tertiary amino group in the β- or γ-position to the ester group. A tertiary amine group, in the β-position to a nitrile group, also has a retarding effect on the Grignard reaction. We could not obtain ketones by the action of an organo-magnesium or organo lithium compound on β-dialkylaminopropionitrile. The original aminonitrile was recovered when the reaction was carried out under mild conditions while the reaction products resinified under drastic conditions (prolonged heating). The action of methylmagnesium iodide on methyl-β-diethylaminopropionate gave β-diethylamino-ethyl-dimethylcarbinol (VI) in 57% yield. However, the action of ethyl-, propyl-, butyl- and isoamylmagnesium bromides gave amino ketones and dehydration products of the expected alcohols in low yields. The reaction of ethyl-β-dimethylaminobutyrate with methylmagnesium iodide and ethylmagnesium bromide proceeded smoothly; the corresponding amino alcohols (VII) and (VIII) were thus formed in 69 and 40% yields respectively. The reaction of ethyl-β-piperidylbutyrate with methylmagnesium iodide gave products of undetermined structure, which boiled with decomposition in a 2 mm vacuum at 160–170°. The substitution of methylmagnesium iodide by methylmagnesium bromide in this reaction made it possible to obtain the expected β-piperidylpropyldimethylcarbinol (IX) in 42% yield.

(I) $R=CH_3$, $R'=CH_3$; (II) $R=C_2H_5$, $R'=CH_3$; (III) $R=C_3H_7$, $R'=CH_3$; (IV) $R=C_4H_9$, $R'=CH_3$; (V) $R=$iso-C_5H_{11}, $R'=CH_3$; (VI) $R=CH_3$, $R'=C_2H_5$; (VII) $R=CH_3$, $R'=CH_3$; (VIII) $R=C_2H_5$, $R'=CH_3$; (IX) $R=CH_3$, $R'_2N=C_5H_{10}N$.

$(CH_3)_2NCH_2CH_2—COR$ (X) $R=C_2H_5$, (XI) $R=C_3H_7$, (XII) $R=C_4H_9$, (XIII) $R=$iso-C_5H_{11}.

All the tertiary amino alcohols obtained by us were readily esterified with acid chlorides into the corresponding esters. Benzoates and phenoxyacetates of tertiary amino alcohols were obtained in yields of up to 97% by the action of benzoyl chloride and phenoxyacetyl chloride in a benzene solution and were tested for anesthetic action in the All-Soviet Scientific Research Institute of Chemistry and Pharmaceutics, in the laboratory of Professor M. D. Mashkovsky.

$$\text{(XIV)}\quad (CH_3)_2NCH_2CH_2\overset{OCOC_6H_5}{\overset{|}{C}}(CH_3)_2 \cdot HCl,$$

$$\text{(XV)}\quad (CH_3)_2NCH_2CH_2\overset{OCOC_6H_5}{\overset{|}{C}}(C_2H_5)_2 \cdot HCl,$$

$$\text{(XVI)}\quad (CH_3)_2NCH_2CH_2\overset{OCOCH_2OC_6H_5}{\overset{|}{C}}(C_2H_5)_2 \cdot HCl,$$

$$\text{(XVII)}\quad (CH_3)_2NCH_2CH_2\overset{OCOC_6H_5}{\overset{|}{C}}(C_3H_7)_2 \cdot HCl,$$

$$\text{(XVIII)}\quad (CH_3)_2NCH_2CH_2\overset{OCOC_6H_5}{\overset{|}{C}}(C_4H_9)_2 \cdot HCl,$$

$$\text{(XIX)}\quad (CH_3)_2NCH_2CH_2\overset{OCOC_6H_5}{\overset{|}{C}}(\text{изо-}C_5H_{11})_2 \cdot HCl,$$

$$\text{(XX)}\quad (C_2H_5)_2NCH_2CH_2\overset{OCOC_6H_5}{\overset{|}{C}}(CH_3)_2 \cdot HCl,$$

$$\text{(XXI)}\quad (CH_3)_2N\overset{CH_3}{\overset{|}{C}}HCH_2\overset{OCOC_6H_5}{\overset{|}{C}}(CH_3)_2 \cdot HCl,$$

$$\text{(XXII)}\quad (CH_3)_2N\overset{CH_3}{\overset{|}{C}}HCH_2\overset{OCOCH_2OC_6H_5}{\overset{|}{C}}(CH_3)_2 \cdot HCl,$$

$$\text{(XXIII)}\quad (CH_3)_2N\overset{CH_3}{\overset{|}{C}}HCH_2\overset{OCOC_6H_5}{\overset{|}{C}}(C_2H_5)_2 \cdot HCl,$$

$$\text{(XXIV)}\quad C_5H_{10}N\overset{CH_3}{\overset{|}{C}}HCH_2\overset{OCOC_6H_5}{\overset{|}{C}}(CH_3)_2 \cdot HCl,$$

$$\text{(XXV)}\quad C_5H_{10}N\overset{CH_3}{\overset{|}{C}}HCH_2\overset{OCOCH_2OC_6H_5}{\overset{|}{C}}(CH_3)_2 \cdot HCl.$$

TABLE 1

Preparation	Activity index (for 1% solution)	Toxicity-mean fatal dose (mg/kg)	Presence of irritating action
Novocaine	69	60	Does not irritate
(XIV) . .	22	26.5	
(XV) . .	20	21.5	
(XVII) .	250	18.5	Irritates
(XVIII) .	192	14.5	
(XIX) .	13	12.5	Does not irritate

TABLE 2

Preparation	Activity index, concentration (in %)				General evaluation
	0.25	0.5	1	2	
Dicaine	1100	1300	1300	Complete	
Novocaine			310		
(XX) . .			790	810	+
(XXI) .		346	670	831	+
(XXII) .	900	980	1050		++
(XXIII) .			449	596	+
(XXIV) .	1165	1150	1230		+++
(XXV) .		555	700		+

The results of the tests for surface anesthesia (by a modification of Renier's method) on the preparations (XIV–XIX) are given in Table 1.

The increase in the radicals, at the tertiary carbon, results at first in an increase in the anesthetic effect of the compound, then to its abrupt decrease. The radicals C_3H_7 and C_4H_9 are optimal. The irritating effect of the preparation increases simultaneously with increase in activity. The toxicity of the compounds in this series increases proportionately to the increase in the radicals at the tertiary carbon atom. The presence of a substitutent (of the methyl group) in the amino group chain has a considerable effect on the anesthetic activity of the compound.

The introduction of a methyl group into the amino alcohol group leads to a sharp increase in anesthetic activity (compounds XIV and XXI, XV and XXIII). The activity also increases on substituting the dimethylamino by the diethylamine group (XIV and XX) and especially by the piperidine group (XXI and XXIV). Phenoxyacetates only in some cases are more active than benzoates, in contrast to the anesthetics of the piperidine series, where this is a strongly held rule. The most interesting compound we prepared was the hydrochloride of β-piperidyl-propyldimethylcarbinol benzoate (XXIV), which is similar in activity to dicaine (Table 2).

EXPERIMENTAL

Ethyl crotonate. 1000 g of acetoacetic ester was hydrogenated without solvent in an autoclave at 125–130° with a hydrogen pressure of 110 atm. in the presence of 40 g of Raney nickel catalyst. From distillation we ob-

tained 660 g of ethyl β-hydroxybutyrate with b.p. 82–92° at 15 mm. To 300 g (2.1 moles) of the ethyl β-hydroxybutyrate obtained was added 234 g (2.3 moles) of acetaldehyde while cooling in ice water. Over 30 minutes, 115 g of acetic acid was distilled off in vacuum, 50 g of fused potassium acetate was added to the residue and 400 g of dry ethyl crotonate with b.p. 135–150° was distilled off. The distilled product was washed with water, a 10% potash solution and again with water and was dried with calcium chloride. On distilling with a fractionating column, we obtained 170 g of ethyl crotonate with b.p. 136–140°. The yield was 43% on the acetoacetic ester.

Methyl β-dimethylaminopropionate. 100 g of methyl acrylate (b.p. 78–80°) was saturated with 62 g of gaseous dimethylamine. The mixture was kept for 24 hours at room temperature. On distilling we obtained 137 g of methyl β-dimethylaminopropionate with b.p. 152–154°. The yield was 90%.

Ethyl β-dimethylaminobutyrate. A mixture of 80 g of ethyl crotonate and 52 g of gaseous dimethylamine was kept for 24 hours at room temperature. On distilling we obtained 105 g of ethyl β-dimethylaminobutyrate with b.p. 85–87° at 27 mm. The yield was 93%.

Methyl β-diethylaminopropionate. A mixture of 86 g of methyl acrylate and 90 g of diethylamine was kept for two days at room temperature. On distilling we obtained 128 g of methyl β-diethylaminopropionate with b.p. 177–181°. The yield was 80%.

Ethyl β-piperidylbutyrate. A mixture of 50 g of ethyl crotonate and 45 g of piperidine was kept for six days at room temperature. On distilling we obtained 65 g of ethyl β-piperidylbutyrate with b.p. 120–122° at 18 mm. The yield was 75%. After one day the reaction went 47%, after 4 days, 66% and after 3.5 months, 76%.

β-Dimethylaminoethyldimethylcarbinol (I). With vigorous stirring and cooling in ice water, 20 g (0.15 mole) of methyl β-dimethylaminopropionate in 50 ml of ether was added to a solution of methylmagnesium iodide (0.45 mole), prepared from 10.8 g of magnesium and 64 g of methyl iodide in 100 ml of absolute ether. The rate of addition was such that the temperature of the reaction mixture did not rise above 5–6°. After adding the aminoester, the mixture was stirred for 3 hours at room temperature and 3 hours while heating on a water bath and then it was hydrolyzed with 50 g of ice and 50 ml of a saturated solution of ammonium chloride. The aqueous layer was saturated with potash and the product was extracted several times with ether, dried with sodium sulfate and distilled in vacuum. We obtained 10.8 g (55%) of (I) as a mobile liquid with an amine odor.

B.p. 55–57.5° at 16 mm, n_D^{20} 1.4305, d_4^{19} 0.8439, MR_D n_D^{19} ; calc. 39.99.
Found %: N 10.52, 10.33. $C_7H_{17}ON$. Calculated %: N 10.67.

The picrate melted at 133–134° after recrystallization from alcohol.

The hydrochloride was very hygroscopic: after 2 recrystallizations from anhydrous alcohol, it melted at 135–138°.

β-Dimethylaminoethyldiethylcarbinol (II) and 1-dimethylaminopentanone-3 (X). The reaction was carried out as described above, starting from 7.9 g of magnesium, 40 g of ethyl bromide, 20 g of methyl β-dimethylaminopropionate and 150 ml of absolute ether. We obtained 8.5 g (35%) of (II).

B.p. 71–73° at 8 mm, n_D^{20} 1.4431, d_4^{20} 0.8578, MR_D 49.15; calc. 49.23.
Found %: N 9.52, 9.24. $C_9H_{21}ON$. Calculated %: N 9.39.

The hydrochloride melted at 159–160° (from alcohol).

Found %: N 6.93, 7.06. $C_9H_{22}ONCl$. Calculated %: N 7.14.

In this experiment we also obtained 4.2 g (21%) of β-dimethylaminopentanone-3 (X) with b.p. 63–67° at 12 mm; n_D^{20} 1.4340.

Found %: N 10.47, 10.58, $C_7H_{15}ON$. Calculated %: N 10.83.

The hydrochloride of the aminoketone (X) was very hygroscopic and quickly deliquesced in air.

The picrate melted at 119–121° after recrystallization from alcohol. A sample mixed with the picrate of the acid melted at 65–89°.

Found %: N 15.98, 16.0. $C_{13}H_{18}O_8N_4$. Calculated %: N 15.67.

β-Dimethylaminoethyldipropylcarbinol (III) and 2-dimethylaminohexanone-3 (XI). With vigorous stirring and cooling in ice water, 25 g (0.19 mole) of methyl β-dimethylaminopropionate in 50 ml of absolute ether was slowly added to an ether solution of propylmagnesium bromide (0.45 mole), prepared from 10.8 g of magnesium and 58 g of propyl bromide in 100 ml of absolute ether. The reaction mixture thickened up strongly and the stirrer stopped. The mixture was boiled vigorously for 5 hours and then was decomposed with 50 g of ice and 100 ml of 18% hydrochloric acid. After extraction of the neutral products with ether, the acidic aqueous solution was saturated with potash and the organic bases were carefully extracted with ether, dried with sodium sulfate and distilled in vacuum. From the low-boiling products we obtained 7.4 g (26%) of (XI).

B.p. 69–71° at 7 mm, n_D^{19} 1.4308, d_4^{19} 0.8600, MR_D 43.01; calc. 43.09.
Found %: N 9.77, 9.65. $C_8H_{17}ON$. Calculated %: N 9.79.

From the high-boiling products we isolated 9.3 g (26%) of (III).

B.p. 83–84° at 4 mm, n_D^{19} 1.4308, d_4^{19} 0.8533, MR_D 58.31; calc. 58.46.
Found %: N 7.35, 7.12. $C_{11}H_{25}ON$. Calculated %: N 7.50.

The picrate melted at 99–100.5° (from alcohol).

β-Dimethylaminoethyldibutylcarbinol (IV) and 1-dimethylaminoheptanone-3 (XII). 20 g (0.15 mole) of methyl β-dimethylaminopropionate in 50 ml of absolute ether was slowly added to an ether solution of butylmagnesium bromide (0.45 mole), prepared from 11 g of magnesium and 70 g of butyl bromide in 100 ml of absolute ether. The reaction was carried out as described in the previous experiment. We obtained 8.5 g (35.5%) of (XII).

B.p. 91–92° at 15 mm, n_D^{20} 1.4290, d_4^{20} 0.8247, MR_D 47.96; calc. 47.41.
Found %: N 8.55, 8.57. $C_9H_{19}ON$. Calculated %: N 8.91.

The picrate melted at 77–78.5° (from alcohol).

Found %: N 14.57, 14.53. $C_{15}H_{22}O_8N_4$. Calculated %: N 14.51.

From the high-boiling products we isolated 7 g (21.3%) of (IV).

B.p. 119–120° at 11 mm, n_D^{17} 1.4490, d_4^{17} 0.8528, MR_D 67.61; calc. 67.70.
Found %: N 6.84, 6.36. $C_{13}H_{29}ON$. Calculated %: N 6.51.

The hydrochloride of the aminoketone (XII) and the aminoalcohol (IV) were white crystals, which quickly deliquesced in air, even after three recrystallizations from acetone.

β-Dimethylaminoethyldiisoamylcarbinol (V) and 1-dimethylamino-6-methylheptanone-3 (XIII). 26 g (0.2 mole) of methyl β-dimethylaminopropionate in 60 ml of absolute ether was slowly added to an ether solution of isoamylmagnesium bromide (0.50 mole), prepared from 12 g of magnesium and 80 g of isoamyl bromide in 120 ml of absolute ether. The reaction was carried out as in the experiment for the preparation of the aminoalcohol (III). We obtained 20 g (61%) of (XIII).

B.p. 78–80° at 3 mm; n_D^{19} 1.4360, d_4^{19} 0.8561, MR_D 52.40; calc. 52.33.
Found %: N 8.44, 8.40. $C_{11}H_{21}ON$. Calculated %: N 8.20.

We also obtained 4.6 g (9.6%) of (V).

B.p. 107–111° at 3 mm, n_D^{17} 1.4490, d_4^{17} 0.8480, MR_D 76.85; calc. 76.93.
Found %: N 6.41, 6.28. $C_{15}H_{33}ON$. Calculated %: N 6.57.

β-Diethylaminoethyldimethylcarbinol (VI). 30 g (0.19 mole) of methyl β-diethylaminopropionate was added to an ether solution of methylmagnesium iodide (0.50 mole), prepared from 12 g of magnesium and 71 g of methyl iodide in 120 ml of absolute ether. The reaction was carried out as in the preparation of the aminoalcohol (I). We obtained 17 g (57%) of (VI).

B.p. 73.5–74.5° at 11 mm, n_D^{20} 1.4266, d_4^{20} 0.8457, MR_D 49.20; calc. 49.22.
Found %: N 8.69, 8.56. $C_9H_{21}ON$. Calculated %: N 8.80.

The hydrochloride melted at 103–105° (from acetone).

β-Dimethylaminopropyldimethylcarbinol (VII). 16 g (0.1 mole) of ethyl β-dimethylaminobutyrate (b.p. 80–82° at 20 mm) in 50 ml of absolute ether was added to an ether solution of methylmagnesium iodide (0.3 mole), prepared from 43 g of methyl iodide and 7.2 g of magnesium in 100 ml of absolute ether. The reaction was carried out as in the preparation of the aminoalcohol (I). We obtained 10 g (69%) of (VII).

B.p. 70–72° at 21 mm, n_D^{23} 1.4266, d_4^{23} 0.8387, MR_D 44.35; calc. 44.31.
Found %: N 9.72, 9.81. $C_8H_{19}ON$. Calculated %: N 9.66.

The picrate melted at 127–129° (from alcohol),

After reprecipitation from alcohol with ether, the hydrochloride came out as long needle-like crystals; they were very hygroscopic and quickly deliquesced in air.

β-Dimethylaminopropyldiethylcarbinol (VIII). 16 g (0.1 mole) of ethyl β-dimethylaminobutyrate in 50 ml of absolute ether was added to an ether solution of ethylmagnesium bromide (0.3 mole), prepared from 33 g of ethyl bromide and 7.2 g of magnesium in 100 ml of absolute ether. The reaction was carried out as described above. We obtained 7 g (40%) of (VII).

B.p. 68–70° at 4 mm, n_D^{24} 1.4390, d_4^{24} 0.8447, MR_D 53.86; calc. 53.84.
Found %: N 8.16, 8.21. $C_{10}H_{23}ON$. Calculated %: N 8.10.

The picrate melted at 117–119° (from alcohol). A sample mixed with the picrate of the acid melted at 72–86°.

Found %: N 14.17. $C_{16}H_{26}O_8N_4$. Calculated %: N 13.91.

The hydrochloride was hygroscopic and deliquesced in air after 3 reprecipitations from alcohol with ether.

β-Piperidylpropyldimethylcarbinol (IX). While the reaction flask was cooled in dry ice and acetone, 33 g (0.16 mole) of ethyl β-piperidylbutyrate (b.p. 108–111° at 13 mm) was slowly added to an ether solution of methylmagnesium bromide (0.50 mole), prepared from 13 g of magnesium and 50 ml of methyl bromide in 150 ml of absolute ether. The reaction was carried out as in the experiment for the preparation of the aminoalcohol (I). We obtained 12.5 g (42%) of (IX).

B.p. 77–79° at 3 mm, n_D^{19} 1.4605.
Found %: N 7.42, 7.39. $C_{11}H_{23}ON$. Calculated %: N 7.56.

The hydrochloride had m.p. 169–171 ° (from acetone).

On carrying out this experiment under similar conditions with methylmagnesium iodide, we obtained a product, which slowly distilled with considerable decomposition in vacuum at 2 mm at about 130° (bath temperature 160–170°).

The benzoate of β-dimethylaminoethyldimethylcarbinol (XIV). With stirring and cooling in ice water, 4.3 g (0.033 mole) of β-dimethylaminoethyldimethylcarbinol (I) in 5 ml of dry benzene was slowly added to a solution of 11 g (0.08 mole) of benzoyl chloride in 10 ml of dry benzene. Noticeable heating up occurred and crystals immediately precipitated. After standing for 2 hours at room temperature, the crystals were pressed out, washed several times with absolute ether and recrystallized from a mixture of acetone and alcohol (10 : 1). We

obtained 8.5 g (96%) of the hydrochloride of the benzoate of β-dimethylaminoethyldimethylcarbinol with m.p. 166.5–168°.

Found %: N 5.46, 5.28. $C_{14}H_{22}O_2NCl$. Calculated %: N 5.17.

8.5 g of the hydrochloride was decomposed with potash solution and we obtained 5 g of the base of the benzoate (XIV) with b.p. 116–117° at 3 mm.

Found %: N 6.23, 6.17. $C_{14}H_{21}O_2N$. Calculated %: N 5.96.

The base was again converted into the hydrochloride with m.p. 166.5–168°.

The benzoate of β-dimethylaminoethyldiethylcarbinol (XV). With shaking and cooling in ice water, a solution of 8 g (0.05 mole) of β-dimethylaminoethyldiethylcarbinol (II) in 5 ml of dry benzene was added to a solution of 21 g (0.15 mole) of benzoyl chloride in 20 ml of dry benzene. After 10–15 minutes crystals began to deposit. The reaction mixture was kept at room temperature for 5 hours, after which, the crystals were pressed out and washed several times with absolute ether. We obtained 15 g (~100%) of the hydrochloride of the benzoate of β-dimethylaminoethyldiethylcarbinol, which melted at 140–141° after recrystallization from acetone.

Found %: N 4.81, 4.71. $C_{16}H_{26}O_2NCl$. Calculated %: N 4.68.

The hydrochloride was converted into the base. We obtained 10 g of the benzoate (XV) with b.p. 136–137° at 4 mm, n_D^{19} 1.5010.

Found %: N 5.39, 5.41. $C_{16}H_{25}O_2N$. Calculated %: N 5.32.

The phenoxyacetate of β-dimethylaminoethyldiethylcarbinol (XVI). A mixture of 5.5 g (0.03 mole) of phenoxyacetyl chloride, 3 g (0.02 mole) of β-dimethylaminoethyldiethylcarbinol (II) and 10 ml of dry benzene was kept at room temperature for 5 hours. After the usual working up, we obtained 5.3 g (87%) of the hydrochloride of the phenoxyacetate (XVI) with m.p. 155–156° [from a mixture of alcohol and acetone (1 : 10)].

Found %: N 4.18, 4.11. $C_{17}H_{28}O_3NCl$. Calculated %: N 4.25.

The benzoate of β-dimethylaminoethyldipropylcarbinol (XVII). The reaction was carried out as described above. In the reaction we used 8.4 g (0.06 mole) of benzoyl chloride and 4.7 g (0.025 mole) of β-dimethylaminoethyldipropylcarbinol in 15 ml of dry benzene. The mixture was kept at room temperature for 15 hours. We obtained 7.3 g (87%) of the hydrochloride of the benzoate (XVII), which melted at 153.5–154.5° after 2 recrystallizations from acetone.

Found %: N 4.55, 4.13. $C_{18}H_{30}O_2NCl$. Calculated %: N 4.28.

The benzoate of β-dimethylaminoethyldibutylcarbinol (XVIII). A mixture of 11.2 (0.08 mole) of benzoyl chloride, 8.2 g (0.05 mole) of β-dimethylaminoethyldibutylcarbinol (IV) and 15 ml of dry benzene was kept at room temperature for 24 hours. After working up in the usual way, we obtained 13 g (93%) of the hydrochloride of the benzoate (XVIII) with m.p. 113–114.5° (from acetone).

Found %: N 3.81, 3.82. $C_{20}H_{34}O_2NCl$. Calculated % N 3.83.

The benzoate of β-dimethylaminoethyldiisoamylcarbinol (XIX). A mixture of 6 g (0.43 mole of benzoyl chloride, 4.1 g (0.17 mole) of β-dimethylaminoethyldiisoamylcarbinol (V) and 15 ml of dry benzene was kept at room temperature for 2 days. After working up in the usual way we obtained 3.5 g (54%) of the hydrochloride of the benzoate (XIX) with m.p. 130–131.5° (after 3 reprecipitations from alcohol with ether).

Found %: N 3.65, 3.50. $C_{22}H_{38}O_2NCl$. Calculated %: N 3.65.

The benzoate of β-diethylaminoethyldimethylcarbinol (XX). A mixture of 14 g (0.1 mole) of benzoyl chloride, 6 g (0.04 mole) of β-diethylaminoethyldimethylcarbinol (VI) and 15 ml of dry benzene was kept overnight at room temperature. After working up in the usual way we obtained 11 g (97%) of the hydrochloride of the benzoate (XX) with m.p. 150-151° (from acetone).

Found %: N 4.77, 4.42. $C_{16}H_{26}O_2NCl$. Calculated %: N 4.68.

7 g of the hydrochloride was converted into the base. We obtained 4.8 g of the benzoate (XX) as a thick liquid with b.p. 133-135° at 5 mm.

Found %: N 5.29, 5.58. $C_{16}H_{25}O_2N$. Calculated %: N 5.33.

The benzoate of β-dimethylaminopropyldimethyl carbinol (XXI). A mixture of 10.5 g (0.08 mole) of benzoyl chloride, 4 g (0.05 mole of β-dimethylaminopropyldimethylcarbinol (VII) and 13 ml of dry benzene was kept for 24 hours at room temperature. We obtained 6.2 g (79.5%) of the hydrochloride of the benzoate (XXI) with m.p. 140-141.5 ° (after 3 reprecipitations from alcohol with ether).

Found %: N 4.70, 4.97. $C_{15}H_{24}O_2NCl$. Calculated %: N 4.90

The phenoxyacetate of β-dimethylaminopropyldimethylcarbinol (XXII). A mixture of 8.5 g (0.05 mole) phenoxyacetyl chloride, 4 g (0.022 mole) of β-dimethylaminopropyldimethylcarbinol (VII) and 10 ml of dry benzene were kept for a day at room temperature. After working up in the usual way, we obtained 6.2 g (78%) of the hydrochloride of the phenoxyacetate (XXII) with m.p. 137-138° (from acetone).

Found %: N 4.67, 4.71. $C_{16}H_{26}O_3NCl$. Calculated %: N 4.67.

The benzoate of β-dimethylaminopropyldiethylcarbinol (XXIII). A solution of 3 g (0.02 mole) of β-dimethylaminopropyldiethylcarbinol (VIII) in 4 ml of dry benzene was slowly added to a solution of 7.3 g (0.05 mole) of benzoyl chloride in 6 ml of dry benzene, cooled in ice water. Crystals of the hydrochloride did not precipitate after standing for two days at room temperature. The benzene was distilled off and the oily residue was treated with absolute ether. The crystalline hydrochloride formed was reprecipitated four times from alcohol with ether. We obtained 3.5 g (64.5%) of the hydrochloride of the benzoate (XXIII) with m.p. 122-123°.

Found %: N 4.62, 4.21. $C_{17}H_{28}O_2NCl$. Calculated %: N 4.47.

The benzoate of β-piperidylpropyldimethylcarbinol (XXIV). A mixture of 5.6 g (0.09 mole) of benzoyl chloride, 3.5 g (0.02 mole) of β-piperidylpropyldimethylcarbinol (IX) and 10 ml of dry benzene was kept for 12 hours at room temperature. After working up in the usual way we obtained 5.6 g (90%) of the hydrochloride of the benzoate (XXIV) with m.p. 178-179° from a mixture of alcohol and acetone (1 : 5). It was readily soluble in water and alcohol but less in acetone.

Found %: N 4.53, 4.40. $C_{18}H_{28}O_2NCl$. Calculated %: N 4.30.

The phenoxyacetate of β-piperidylpropyldimethylcarbinol (XXV). A mixture of 7 g (0.04 mole) of phenoxyacetyl chloride, 3.5 g (0.02 mole) of β-piperidylpropyldimethylcarbinol (IX) and 10 ml of dry benzene was kept for a day at room temperature and then treated in the usual way. After 3 recrystallizations from acetone, we obtained 2.8 g (40%) of the hydrochloride of the phenoxyacetate (XXV) with m.p. 125-126.5° as fine, flaky crystals, which were readily soluble in water and alcohol and less in acetone.

Found %: N 4.20, 4.34. $C_{19}H_{30}O_3NCl$. Calculated %: N 3.94.

SUMMARY

A series of tertiary γ-dialkylaminopropanols and γ-dialkylaminobutanols was prepared by the Grignard method from the esters of β-dialkylaminopropionic and β-dialkylaminobutyric acids. A series of aminoketones

– intermediate products of the Grignard synthesis – were obtained by carrying out the Grignard reaction with methyl-β-dimethylaminopropionate. The yield of the ketone increased with the size of the radical of the organo-magnesium compound. The tertiary amino alcohols obtained were readily esterified (in 90-100% yield) with benzoyl chloride and phenoxyacetyl chloride.

Some benzoates and phenoxyacetates of tertiary γ-dialkylaminobutanols have a high anesthetic activity similar to the activity of dicaine.

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SYNTHESIS AND REACTIONS OF α- METHYLVINYL ETHERS OF ISOALCOHOLS AND ETHYLENE GLYCOLS. V.

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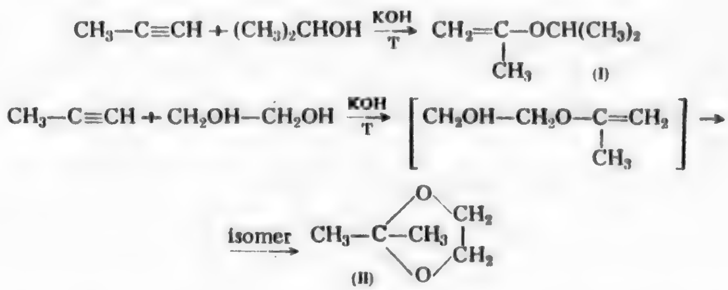
The purpose of this investigation was to synthesize and investigate certain properties of α-methylvinyl isoalkyl ethers and α-methylvinyl ethers of ethylene glycols.

The synthesis of these ethers was carried out using the reaction of methylacetylene in the presence of potassium hydroxide according to the scheme:



In comparing the reaction conditions of the addition of alcohols of the aliphatic series to acetylene [1] and methylacetylene [2] it was observed that the reaction proceeded in the first case at 150–180° using 5–10% potassium hydroxide and in the second case at 240–250° in the presence of 15–20% of the catalyst mentioned. Apparently, the change from acetylene, containing two symmetrical labile hydrogen atoms to substituted acetylenes made the addition more difficult due to the fact that the vinylating agent was no longer the methylacetylene $CH_3C{\equiv}CH$, but its isomer $CH_2{=}C{=}CH_2$ allene [3], which is less active. Therefore, a higher reaction temperature and a larger percent of catalyst was required and this caused a series of side reactions.

We obtained the following α-ethers: α-methylvinyl isopropyl (I), α-methylvinyl isobutyl (III) and α-methylvinyl isoamyl (IV). The boiling points, specific weights and refractive indices of the above ethers are lower than those of the α-methylvinyl alkyl ethers of normal structure [4].

(III) (IV)

When we examined the addition of methylacetylene to ethylene glycol, a cyclic ketal (II) was obtained instead of the expected mono- and di-α-substituted vinyl ethers of ethylene glycol, as are produced in the reaction of ethylene glycol with acetylene [5]. This phenomenon is explained by the fact that the addition of ethylene glycol to methylacetylene occurs at 130–140°, while the addition of ethylene glycol to methylacetylene occurs at 170–180°. Due to the high reaction temperature, the monovinyl ether formed was wholly isomerized into a cyclic ketal. A ketal of such structure had been obtained earlier by other methods [6].

The reactivity of α-methylvinyl isoalkyl ethers was further studied in hydrolysis and polymerization reactions. It was shown that these compounds were very readily hydrolized with 1–2% H_2SO_4.

$$\underset{(I)}{CH_2{=}\underset{\displaystyle CH_3}{\underset{|}{C}}{-}OCH(CH_3)_2} \xrightarrow[H_2SO_4]{HOH} CH_3COCH_3 + (CH_3)_2CHOH$$

We used this reaction to prove the structure of the α-methylvinyl isoalkyl ethers.

α-Methylvinyl isoalkyl ethers were polymerized in the presence of the ionic catalyst $FeCl_3$ (5% dioxane solution). The effect of this catalyst in the first stage of the reaction is expressed as follows:

$$FeCl_3 + HOH \longrightarrow FeCl_3 \cdot HOH \longrightarrow (FeCl_3 \cdot OH) + H^+$$

The proton H^+ participates in the formation of the carbonium ion :

$$CH_2{=}\underset{\displaystyle CH_3}{\underset{|}{C}}{-}OCH_2CH(CH_3)_2 + H^+ \longrightarrow CH_3{-}\underset{\displaystyle CH_3}{\underset{|}{C^+}}{-}OCH_2{-}CH(CH_3)_2$$

The carbonium ion formed leads the polymerization process :

$$CH_3{-}\underset{\displaystyle CH_3}{\underset{|}{C^+}}{-}OCH_2{-}CH(CH_3)_2 + nCH_2{=}\underset{\displaystyle CH_3}{\underset{|}{C}}{-}OCH_2{-}CH(CH_3)_2 \longrightarrow$$

$$\longrightarrow CH_3{-}\underset{CH_3}{\overset{OCH_2CH(CH_3)_2}{C}}{-}\left[{-}CH_2{-}\underset{CH_3}{\overset{OCH_2-CH(CH_3)_2}{C}}{-}\right]_{n-1}{-}CH_2{-}\underset{CH_3}{\overset{OCH_2CH(CH_3)_2}{C}}{-}\cdots$$

The polymerization of α-substituted vinyl ethers of both normal and iso structure occurs below zero, while vinyl alkyl ethers polymerize at the boiling point [7]. The reason for this difference we considered to be the different stability of the oxonium complexes of these compounds (A and B).

$$\underset{(A)}{CH_2{=}CH\underset{\displaystyle H(FeCl_3 \cdot OH)}{\underset{|}{O}}R} \qquad \underset{(B)}{CH_2{=}\underset{\displaystyle CH_3}{\underset{|}{C}}{-}\underset{\displaystyle H(FeCl_3 \cdot OH).}{\underset{|}{O}}R}$$

Complex (B) is more unstable and its formation and dissociation start at a lower temperature.

EXPERIMENTAL

Starting materials and method of synthesis. The starting materials for the synthesis of α-substituted vinyl isoalkyl ethers were alcohols with the following constants: isopropyl b.p. 81–82°, d_4^{20} 0.7800, n_D^{20} 1.3771; isobutyl b.p. 108.6°, d_4^{20} 0.8020, n_D^{20} 1.3980; isoamyl b.p. 131.4°, d_4^{20} 0.8106, n_D^{20} 1.4084; glycol b.p. 196–198°, d_4^{20} 1.1135, n_D^{20} 1.4320. As a monosubstituted acetylenic hydrocarbon, we used methylacetylene, which was prepared by brominating propylene and then splitting out two molecules of hydrogen bromide [8]. The methylacetylene was collected in a weighed receiver, which was placed in a Dewar flask filled with dry ice. The synthesis was carried out in an autoclave, which was cooled to 0–2° (snow). A definite amount of methylacetylene, weighed into an ampule, was cooled in dry ice and together with the ampule was placed in the autoclave, containing alcohol and alkali.

Synthesis of α-methylvinyl isopropyl ether (I). Into a rotating Bergins autoclave of 1 liter capacity, fitted with an electrical heater, a thermometer and an acetylene manometer, by the method given above, we loaded 120 g (3 mole) of methylacetylene, 198 g (2 mole) of isopropyl alcohol and 66 g (20%) of powdered potassium hydroxide. The autoclave was heated for 11 hours at 240–248°. The maximum pressure in the autoclave was 75–80 atm. Before unloading the autocalve was cooled. The methylacetylene, which had not reacted with alcohol, was collected in a trap in a Dewar flask with carbon dioxide. We recovered 22.8 g of methylacetylene. The residual reaction mixture was transferred from the autoclave into a flask. The reaction mixture was distilled in a flask with a pear fractionating column. The following fractions were collected: 1st-61–78° (754 mm), 157.2 g; 2nd-78–82° (756 mm), 60.2 g. A large oily residue (42.4 g) was left in the flask.

The 1st fraction was dried with fused potash and distilled on a column with an efficiency of 20 theoretical plates.

B.p. 77–78.5° (756 mm), n_D^{20} 1.3932, d_4^{20} 0.7691, MR_D 30.7; calc. 31.08.
Found %: C 72.22; H 12.19. M 97.0. $C_6H_{12}O$. Calculated %: C 72.00; H 12.00. M 100.

After a second distillation of the 2nd fraction we isolated a substance with b.p. 80–82°, n_D^{20} 1.3770, d_4^{20} 0.7803, which was unreacted isopropyl alcohol. The yield of ether (I) was 54.2%.

Hydrolysis of α-methylvinyl isopropyl ether. Into a conical flask with a ground stopper was placed a sample of the substance weighing 16.2 g and 30 ml of a 2% solution of H_2SO_4. The reaction mixture was shaken mechanically at room temperature for 1 hour, after which the acid was neutralized with fused potash and the hydrolysis product was distilled on a water bath in a flask with a pear fractionating column. In this way, we obtained a fraction with b.p. 54–83°, which was a mixture of acetone and isopropyl alcohol. On treating this mixture with 2,4-dinitrophenylhydrazine, yellow-orange crystals precipitated, which, after two recrystallizations from alcohol, had m.p. 127.5° and corresponded to acetone 2,4-dinitrophenylhydrazone. A mixed m.p. was not depressed (literature data [9], m.p. 128°).

Synthesis of α-methylvinyl isobutyl ether (III). Into the autoclave was loaded 130 g (3 mole) of methylacetylene, 228 g (2 mole) of isobutyl alcohol and 74 g of potassium hydroxide (20%). The autoclave was heated for 13 hours at 240–250° and then cooled to room temperature, when the unreacted methylacetylene was collected in a trap in a Dewar flask filled with carbon dioxide. We recovered 4.2 g of methylacetylene. The reaction mixture was distilled in a flask with a pear fractionating column. The following fractions were collected: 1st-b.p. 51–104° (749 mm), 196.6 g; 2nd-b.p. 104–110° (749 mm), 40.6 g. A large oily residue (39.3 g) was left in the flask. The 1st fraction was washed 6 times with water and dried with fused potash. After a second distillation on a column it had:

B.p. 98.5–99° (749 mm), n_D^{20} 1.4050, d_4^{20} 0.7817, n_D^{20} 34.49; calc. 34.8.
Found %: C 71.07; H 12.65. M 109, 111. $C_7H_{14}O$. Calculated %: C 71.17; H 12.4. M 114.

The 2nd fraction was dried and again distilled at 106–108° (749 mm), n_D^{20} 1.3940, d_4^{20} 0.8022 and was isobutyl alcohol. The yield of ether (III) was 51.6%.

Hydrolysis of α-methylvinyl isobutyl ether was carried out under the conditions described above. We obtained a 2,4-dinitrophenylhydrazone with m.p. 127°.

Synthesis of α-methylvinyl isoamyl ether (IV). Into an autoclave of capacity 0.5 liter was loaded 123 g (1.5 mole) of isoamyl alcohol, 80 g (2 mole) of methylacetylene and 37 g of potassium hydroxide (20%). The autoclave was heated for 9 hours at 240–250°. After cooling, the autoclave to room temperature, the unreacted methylacetylene was collected. We recovered 2.7 g. On distilling, we collected the following fractions: 1st-b.p. 121–127° (751 mm), 88.8 g; 2nd-b.p. 127–132° (751 mm), 17.7 g; a large tarry residue remained in the distilling flask (44.2 g). The 1st fraction was washed 4 times with water, dried with fused potash and distilled a second time on a column.

B.p. 126–127° (749 mm), d_4^{20} 0.7771, n_D^{20} 1.4172, MR_D 39.8; calc. 40.3.
Found %: C 76.32; H 12.7. M 124. $C_8H_{16}O$. Calculated %: C 76.2; H 12.4. M 128.

The 2nd fraction was again distilled at b.p. 130–131° (749 mm), n_D^{20} 1.4320, d_4^{20} 0.8104 and was isoamyl alcohol. The yield of the ether (IV) was 50.7%.

Hydrolysis of α-methylvinyl isoamyl ether was carried out under the conditions described above. We obtained acetone 2,-4-dinitrophenylhydrazone with m.p. 127–129°.

The vinylation of ethylene glycol. Into an autoclave of capacity 0.5 liter was loaded 124 g (2 mole) of ethylene glycol, 100 g (3 mole) of methylacetylene and 32.4 g of potassium hydroxide (20%). The autoclave was heated for 8 hours at 170–175°, after which the autoclave was cooled to room temperature and unreacted methylacetylene was collected. We collected 5.7 g. The reaction mixture was distilled on a Wood's metal bath in a flask with a pear condenser. The following fractions were collected: 1st-b.p. 70–94° (751 mm), 166.8 g; 2nd-b.p. 91–93° (9 mm), 81.2 g. A large tarry residue (11.7 g) was left in the distillation flask. The 1st fraction was dried with fused potash and after treatment with metallic sodium had:

B.p. 88.5–89° (749 mm), n_D^{20} 1.3970, d_4^{20} 0.9259, MR_D 25.01; calc. 25.37.

Found %: C 58.94; H 9.77. M 103.7, 105. $C_5H_{10}O_2$. Calculated %: C 58.8; H 9.8. M 102.

The 2nd fraction with b.p. 91–93° (9 mm), n_D^{20} 1.4322, d_4^{20} 1.116 was unreacted ethylene glycol. The yield of the cyclic ketal of ethylene glycol (II) was 81.3%.

The polymerizations of α-methylvinyl ethyl and α-methylvinyl isoalkyl ethers were carried out in a three-necked flask, fitted with a mechanical stirrer, a reflux condenser and a thermometer. Into the flask was loaded 0.1–0.2 mole of the α-ether. After cooling to −15 to −25°, 0.015g of $FeCl_3$ (5% dioxane solution) was added with vigorous stirring. Immediately an exothermal reaction began. The reaction mixture then thickened up and the temperature of the reaction rose to 0°. Then there began a slow lowering of the temperature to −15 to −17°; at this, the reaction was complete. The polymer obtained was soluble in ether or acetone and was precipitated from these solutions by methanol. Decantation separated the main mass of the solvent from the polymer, after which, the polymer was dried to constant weight at 50–60° in vacuum (20–25 mm). The determination of the viscosity η (in centipoises) was carried out at 20° in an Ostwald viscometer. The results of the experiments and the properties of the polymers obtained are given in the table.

Name of α-ether	Sample of α-ether (in g)	Amt. of $FeCl_3$ (5% solun. in dioxane) (in g)	Reaction temperature	Yield polymer (in %)	Characteristics of polymers	Prop. of polymers			Found (%)		Calculated (%)	
						n_D^{20}	η_{20}	M	C	H	C	H
α-Methylvinyl ethyl ether ($C_5H_{10}O$)	20	0.015	From −22 to −25°	96.6	Transparent, solid polymer	—	0.8336	4876.5007	69.48	11.33	69.7	11.63
α-Methylvinyl isopropyl ether ($C_6H_{12}O$)	20	0.015	From −17 to −20	94.3	Very viscous, transparent liquid	1.4678	0.9702	4807.5170	72.20	12.19	72.00	12.00
α-Methylvinyl isobutyl ether ($C_7H_{14}O$)	11.2	0.015	From −15 to −17	95.1	Transparent, solid polymer	—	0.8642	5809.5900	76.26	12.70	76.24	12.41

* The polymers were soluble in ether, acetone, benzene, toluene, benzene, dioxane and other organic solvents.

SUMMARY

1. The reaction of methylacetylene with isopropyl, isobutyl and isoamyl alcohols in the presence of potassium hydroxide powder resulted in the formation of the corresponding substituted vinyl ethers: α-methylvinyl isopropyl, isobutyl and isoamyl.

2. The reaction of methylacetylene with ethylene glycol in the presence of potassium hydroxide resulted in the formation of the monovinyl ether of ethylene glycol, which, at the high temperature of the reaction, was isomerized into a cyclic ketal.

3. The structure of the α-methylvinyl isoalkyl ethers was

proved by hydrolysis with 2% H_2SO_4. The hydrolysis products were isolated and characterized.

4. The polymerization conditions were found for α-methylvinyl ethyl, isopropyl and isobutyl ethers with $FeCl_3$ catalysts (5% solution in dioxane). The polymers obtained were characterized.

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CONFIGURATION AND PROPERTIES OF UNSATURATED ACIDS AND THEIR DERIVATIVES

VI. THE REACTIVITY OF STEROISOMERIC CROTONIC ACIDS AND THEIR ESTERS

A. K. Plisov and A. V. Bogatsky

One of us had shown earlier [1–5] that the reactivity of geometrically isomeric unsaturated acids depended essentially on their structure. The acids and their esters behave differently on hydrolysis, oxidation and saponification depending on whether they have a cis- or trans-structure. It is particularly interesting that in the majority of the above cases, the effect of the size of the alcohol radical on the reactivity of the esters was also clearly noticeable. These facts are in agreement with the data found in the literature on this problem and obtained independently of the work of the authors of this article [6–12].

As the above facts were obtained only by studying such acids as oleic, elaidic, petroselinic, petroelaidic and cis- and trans-cinnamic acids, it seemed extremely interesting to study stereoisomeric crotonic acids as the simplest acids in the series of monobasic unsaturated and steroisomeric acids.

The esters of crotonic acids have not been studied from this point of view. In connection with the acids, themselves, Paal and Schiedevitz [9], in studying the hydrogenation of these acids, used products which they themselves said were not completely pure and their work should be checked, while the conditions under which the experiments were carried out did not, according to us, achieve complete equality of the conditions of hydrogenation.

Due to this, we decided to undertake an investigation of the relation of the reactivity of crotonic acids and their esters to their structures. It also seemed interesting to examine the effect of the various alcohol radicals in the ester group on this process. Besides this, we hoped to settle the problem of the structure of these acids as now, after the recent investigations by Nesmeyanov [13] which showed that the work by Auwers and Wissebach [14] was incorrect, the problem of proving their structure chemically, remained unsolved.

The results of the experiments carried out were in full agreement with those data which were obtained earlier for other purposes. It was shown that cis- trans-isomeric crotonic acids have different reactivity in reactions at the double bond. Such a difference is wholly in agreement with the concepts of steric hindrance. Crotonic acid with m.p. 72° (trans-isomer) is hydrogenated more slowly than isocrotonic acid with m.p. 14° (cis-isomer). All the crotonic esters are likewise hydrogenated more slowly than the corresponding esters of isocrotonic acid.

Such a difference in rates may be explained by the fact that in the case of the trans-isomers the methyl radical and the carboxyl (or ester) group, are situated on opposite sides of the double bond, and make it more difficult for the reagents to reach this spot than in the case of the cis-isomer where both groups are situated at one side of the plane of the double bond.

EXPERIMENTAL

Preparation of crotonic acids and their esters. Trans-crotonic acid with m.p. 72° was prepared by us by the well-known method of condensing acetaldehyde with malonic acid in the presence of pyridine.

Cis-crotonic acid (isocrotonic acid) with m.p. 14° was prepared by a sodium amalgam reduction of β-chloro-isocrotonic acid, which in its turn was prepared by treating acetoacetic ester with phosphorus pentachloride. In carrying out this synthesis we succeeded in raising the yield of isocrotonic acid in comparison with yields reported in previous papers [15, 16]. The pure isocrotonic acid had b.p. 55–56° (5 mm), 62–64° (10 mm), m.p. 14° and n_D^{20} 1.4450.

The methyl ester of crotonic acid was prepared by normal esterification, by heating the crotonic acid with anhydrous methyl alcohol in the presence of concentrated sulfuric acid. The butyl, isobutyl and isoamyl esters of crotonic acid were prepared by a similar method.

The benzyl ester of crotonic acid, which had not been described previously in the literature, was prepared by heating the potassium salt of crotonic acid for several hours with benzyl chloride in anhydrous methyl alcohol [17]. The ester was a colorless liquid with an odor reminiscent of mushrooms.

Methyl isocrotonate was prepared by reacting the silver salt of isocrotonic acid with methyl iodide. The butyl, isobutyl and isoamyl esters of isocrotonic acid, which had not been described in the literature previously, were prepared from the silver salt of isocrotonic acid and butyl, isobutyl and isoamyl bromides, respectively. These esters were colorless liquids with pleasant, flower-like odors, which were soluble in alcohol, ether and glacial acetic acid.

The benzyl ester of isocrotonic ester, which had also not been described in the literature, was prepared similarly to the benzyl ester of crotonic ester. To avoid isomerization by heat, the temperature of the bath on which the potassium crotonate was heated with benzyl chloride in anhydrous methyl alcohol, did not rise above 70°.

TABLE 1

Physical Constants of the Esters of Crotonic and Isocrotonic Acids

R	Esters of crotonic acid		Esters of isocrotonic acid	
	boiling point	n_D^{20}	boiling point	n_D^{20}
CH_3	121°	1.4230	118°	1.4175
n-C_4H_9 . .	178–180	1.4283	62 (at 12 mm) 80–83 (at 42 mm)	1.4280
iso-C_4H_9 .	171	1.4220	56 (at 8 mm) 58 (at 12mm)	1.4185
iso-C_5H_{11} .	182–185	1.4265	74–76 (at 21mm)	1.4250
$C_6H_5CH_2$.	125 (at 5mm) 138 (at 12mm)	1.5180	121–122 (at 10mm)	1.5110

The ester was a colorless liquid with a characteristic odor, reminiscent of mushrooms. It dissolved in alcohol, ether and glacial acetic acid.

Hydrogenation of crotonic acids. For hydrogenation, equal samples of the crotonic acids (0.00058 mole), dissolved in anhydrous ethyl alcohol (4 ml) were placed in identical vessels for hydrogenation ("buckets"), into which had been placed, equal samples of the catalyst – palladium, precipitated on $BaSO_4$ (0.02 g of Pd/$BaSO_4$, which corresponded to 0.00052 g of metallic palladium). The vessels for hydrogenation with the samples were placed in the apparatus for shaking. Hydrogen, purified by a suitable method, was introduced into these vessels under slight, identical pressures.

The hydrogenation of the acids was carried out at two temperatures (11 and 22°) in ethyl alcohol on a Pd catalyst (see Tables 2 and 3), and also on a Pt catalyst at 22° in anhydrous ethyl alcohol and on a Pt catalyst at 22° in glacial acetic acid (see Tables 4 and 5). In all cases, it is noticeable that the isocrotonic acid is hydrogenated appreciably faster than the crotonic acid, which confirms the idea of the cis-configuration of the first and the trans-configuration of the latter.

TABLE 2

Course of the Hydrogenation of Crotonic and Isocrotonic Acids at 22° on a Palladium Catalyst in Anhydrous Ethyl Alcohol

Time (in minutes)	Crotonic acid		Isocrotonic acid	
	H_2 absorbed (%)	$\Delta P/\Delta t$	H_2 absorbed (%)	$\Delta P/\Delta t$
10	14.0	1.4	38.0	3.8
20	21.6	0.7	67.6	3.0
40	40.3	0.7	98.6	2.4
90	62.0	0.4	100	0
120	74.8	0.4	—	—
180	97.1	0.4	—	—
240	100	0	—	—

TABLE 3

Course of the Hydrogenation of Crotonic and Isocrotonic Acids at 11° on a Palladium Catalyst in Anhydrous Ethyl Alcohol

Time (in minutes)	Crotonic acid		Isocrotonic acid	
	H_2 absorbed (%)	$\Delta P/\Delta t$	H_2 absorbed (%)	$\Delta P/\Delta t$
10	6.8	0.7	30.0	3.0
20	9.8	0.3	60.5	3.0
40	15.9	0.2	95.8	1.3
90	25.8	0.2	100	0
120	30.0	0.14	—	—
180	40.1	0.14	—	—
240	48.5	0.14	—	—
660	100	0	—	—

TABLE 4

Course of the Hydrogenation of Crotonic and Isocrotonic Acids at 22° on a Platinium Catalyst in Anhydrous Ethyl Alcohol

Time (in minutes	Crotonic acid		Isocrotonic acid	
	H_2 absorbed (%)	$\Delta P/\Delta t$	H_2 absorbed (%)	$\Delta P/\Delta t$
10	14.0	1.4	38.0	3.8
20	20.0	0.7	73.2	3.7
40	38.0	0.7	97.2	1.0
90	76.0	0.7	100	0
120	90.0	0.5	—	—
180	97.2	0.1	—	—
240	100	0	—	—

TABLE 5

Course of the Hydrogenation of Crotonic and Isocrotonic Acids at 22° on Palladium Catalyst in Glacial Acetic Acid

Time (in minutes	Crotonic acid		Isocrotonic acid	
	H_2 absorbed (%)	$\Delta P/\Delta t$	H_2 absorbed (%)	$\Delta P/\Delta t$
10	4.1	0.4	27.5	2.7
20	6.2	0.2	42.0	1.4
40	11.1	0.2	70.0	1.4
60	16.6	0.1	85.4	0.8
120	25.0	0.1	100	0
180	31.2	0.1	—	—
360	48.0	0.1	—	—
780	93.0	0.07	—	—
900	100	0	—	—

Hydrogenation of esters of crotonic acids. The experiments on the hydrogenation of the esters of crotonic acids were carried out exactly like the experiments on the hydrogenation of the acids themselves, using equimolecular amounts of the respective esters (0.00058 mole) and the same amounts of anhydrous alcohol and Pd/$BaSO_4$. The catalyst was first saturated with hydrogen. The apparatus in which the esters were hydrogenated was constructed so that the hydrogenation of 5 pairs of esters was carried out at the same time. With this arrangement, the experiments were carried out with exactly equal conditions, which made it possible to arrive at conclusions on the effect of the size and the structure of the alcohol radical on the course of the reaction.

TABLE 6

Course of the Hydrogenation of Esters of Crotonic and Isocrotonic Acids at 22° on a Palladium Catalyst in Anhydrous Ethyl Alcohol

Time (in min)	Esters of crotonic acid									
	methyl		butyl		isobutyl		isoamyl		benzyl	
	P	ΔP/Δt	P	ΔP/Δt	P	ΔP/Δt	P	ΔP/Δt	P	ΔP/Δt
10	20.8	2.0	11.4	1.1	13.4	1.3	12.3	1.2	12.3	1.2
20	39.0	1.8	22.5	1.1	32.4	1.3	24.6	1.2	21.7	0.9
40	70.0	1.5	53.5	1.1	59.5	1.3	43.5	1.0	38.4	0.8
60	88.8	0.9	76.0	1.1	74.7	0.8	56.5	0.6	45.6	0.6
90	93.0	0.5	84.5	0.4	87.3	0.4	71.0	0.5	68.1	0.6
120	100	0	90.5	0.2	91.5	0.1	75.3	0.2	76.1	0.3
180	—	—	97.2	0.1	98.6	0.1	87.0	0.2	84.0	0.1
240	—	—	100	0	100	0	100	0	92.3	0.1
300	—	—	—	—	—	—	—	—	100	0

Time (in min)	Esters of isocrotonic acid									
	methyl		butyl		isobutyl		isoamyl		benzyl	
	P	ΔP/Δt	P	ΔP/Δt	P	ΔP/Δt	P	ΔP/Δt	P	ΔP/Δt
10	28.0	2.8	25.0	2.5	22.0	2.2	21.4	2.1	27.5	2.7
20	49.3	2.1	49.3	2.4	43.0	2.4	40.7	1.9	40.6	1.3
40	75.0	1.2	74.3	1.2	73.6	1.5	72.8	1.6	52.1	—
60	90.1	1.7	94.4	1.0	88.8	0.7	88.5	0.7	75.4	1.1
90	100	0	100	0.4	100	0.3	99.2	0.3	87.0	0.4
120	—	—	100	0	100	0	100	0	100	0
180	—	—	—	—	—	—	—	—	—	—
240	—	—	—	—	—	—	—	—	—	—
300	—	—	—	—	—	—	—	—	—	—

In Table 6 we give data on the hydrogenation of the esters of both acids at 22°. It is noticeable that the effect of the size of alcohol radical is shown with greater clarity by the esters of the trans-isomer (crotonic acid) than by the esters of the cis-isomer (isocrotonic acid). In all cases the esters of crotonic acid were hydrogenated more slowly than the esters of isocrotonic acid, which makes it possible to ascribe to the first, a trans-and the second a cis-structure.

SUMMARY

1. The butyl, isobutyl, isoamyl and benzyl esters of isocrotonic acid and benzyl ester of crotonic acid were synthesized and their properties described.

2. The difference in the relative hydrogenation rates of crotonic and isocrotonic acids was established : isocrotonic acid adds hydrogen more readily.

3. The difference in the relative hydrogenation rates of esters of crotonic and isocrotonic acids was established: the esters of isocrotonic acid add hydrogen more readily.

4. It was shown that the difference in hydrogenation rates of crotonic and isocrotonic acids still remained when the reaction was carried out with various catalysts (platinum, palladium), in various solvents (alcohol, acetic acid) and at various temperatures.

5. It was established that an increase in the alcohol radical in the ester group resulted in a decrease in the relative rate of hydrogen addition, furthermore, this difference was made more noticeable by comparing the various esters of crotonic acid.

6. The difference in the relative hydrogenation rates, confirmed that isocrotonic acid and its esters have a cis-structure and crotonic acid and its esters have a trans-structure.

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INVESTIGATION IN THE FIELD OF CONJUGATED SYSTEMS

LXXII. HYDROGENATION OF ALKENYLACETYLENES

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In hydrogenating vinylalkylacetylenes (I) over colloidal palladium, the addition of hydrogen takes place first of all at the triple bond with the formation of diene hydrocarbons: however, the reaction does not end there and a large portion of the diene hydrocarbons undergo further hydrogenation to the corresponding olefins. The curves of the rates of hydrogenation of vinylalkylacetylenes have a break only after the addition of 2 moles of hydrogen [1].

It seemed interesting to study hydrogenation under the same conditions of vinylacetylene homologs of different structure and in particular, hydrocarbons of type (II) and (III).

$$R{-}C{\equiv}C{-}CH{=}CH_2 \qquad HC{\equiv}C{-}CH{=}CH{-}R \qquad HC{\equiv}C{-}\underset{\displaystyle R}{\underset{|}{C}}{=}CH_2.$$

(I) (II) (III)

According to the literature data, in hydrogenating one of the hydrocarbons of type (III) — isopropenylacetylene — over colloidal palladium, the hydrogenating rate was observed to change somewhat after the addition of one hydrogen molecule and it was concluded from this that simultaneously with isopropenylacetylene, isoprene formed from it was also hydrogenated to a certain extent [2]. Isoprene was obtained in good yield by hydrogenating isopropenylacetylene over active iron under pressure [3].

Hydrogenation over colloidal palladium of two hydrocarbons of the type (II) — propenylacetylene (penten-3-ine-1) and butenylacetylene (hexen-3-ine-1), as well as of type (III) — isopropenylacetylene (2-methylbuten-1-ine-3), which we carried out showed that a considerably greater selectivity exists in the hydrogenation process in the case of vinylacetylene hydrocarbons with a terminal acetylene group (II and III) than in the case of vinylalkylacetylenes (I).

A break in the curve of the hydrogenation rate of propenyl- and butenylacetylenes was observed in the region corresponding to the absorption of 1 mole of hydrogen for each mole of alkenylacetylene. These homologs differ little in hydrogenation rates which are considerably less than those of vinylakylacetylenes (I).

Isopropenylacetylene is hydrogenated at a somewhat greater rate than propenylacetylene. The breaks in the curves of hydrogenation rate of these isomers are approximately in the same region.

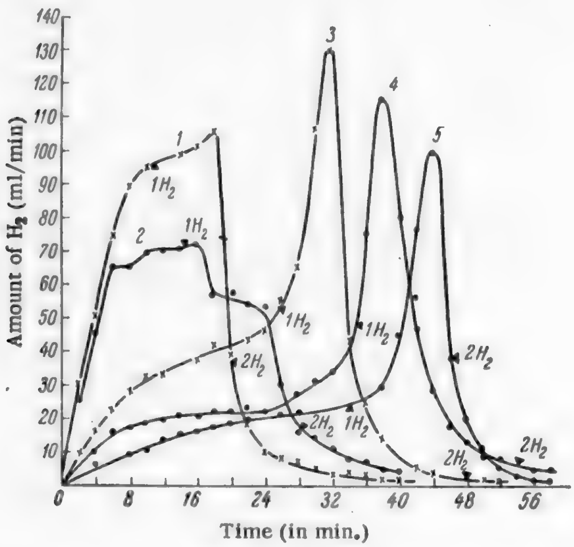
A graphic impression of the hydrogenation process in all the cases investigated may be obtained by examining the figure.

By hydrogenating propenyl-, isopropenyl- and butenylacetylene with a ratio of 1 mole hydrogen to 1 mole of material, the corresponding diene hydrocarbons are mainly formed. Very small amounts of olefins are found in the reaction products. The composition of the hydrogenation products was determined by the ratio between the amount of di- and tetrabromides, formed when these products were brominated in chloroform. As the dibromides were obtained in very small amounts, we usually collected them over a large temperature range and did not subject them to further purification from the small traces of tetrabromides. The amount of the latter in

the dibromides could be calculated on the basis of analytical data for bromine.

The isoprene in the hydrocarbon mixture obtained by hydrogenating isopropenylacetylene, was determined as tetrabromide and by its condensation product with maleic anhydride. The yield of 4-methyl-Δ^4-tetrahydrophthalic acid was about 80%, which agrees well with the bromination data.

The comparative data on the composition of the hydrogenation products is given in Table 1. It can be seen from the table that piperylene and hexadiene-1,3, formed by hydrogenating propenyl- and butenylacetylenes, underwent further hydrogenation (to olefins) but to a much smaller degree than the same hydrocarbons obtained by hydrogenating vinylmethyl- and vinylethylacetylenes under the same conditions.



The dynamics of hydrogenation.
1. Vinylethylacetylene; 2. vinylmethylacetylene;
3. isopropenylacetylene; 4. propenylacetylene;
5. butenylacetylene.

The same selectivity existed in the hydrogenation of acetylene alcohols with a terminal acetylene group [4].

As is known, the ethylene bond is hydrogenated much more readily than the acetylene [5]. The initial hydrogenation of the acetylene bond in the case of vinylacetylene hydrocarbons is due to the heterogeneous character of the reaction: the hydrocarbon is absorbed on the catalyst mainly at the acetylene bond.

TABLE 1

Hydrocarbon	Found in hydrogenation products (%)	
	diolefin	olefin
$HC\equiv C-CH=CH-CH_3$ . . .	90	10
$HC\equiv C-C(CH_3)=CH_2$	80	20
$CH_3-C\equiv C-CH=CH_2$ . . .	65	35
$HC\equiv C-CH=CH-CH_2-CH_3$	90	10
$CH_3-CH_2-C\equiv C-CH=CH_2$.	45	55

In the hydrogenation of hydrocarbons of type (II) and (III), all the surface of the catalyst with the capacity of absorbing hydrocarbons, appears to be occupied by acetylene groupings of alkenylacetylenes up to the moment of their almost complete conversion into diene hydrocarbons. Then, this surface is freed and the hydrogenation of the diene hydrocarbons proceeds at a considerably greater rate.

However, in the case of vinylalkylacetylenes (I) a lower difference in the capacity for absorption on palladium is observed between the original materials and their hydrogenation products— the diene hydrocarbons; therefore, both are hydrogenated and the hydrogenation process loses its selectivity. The lower tendency for absorption on palladium of vinylalkylacetylenes (I) in comparison with that of alkenylacetylenes (II and III) is apparently due to steric hindrance.

It should be noted, that in the hydrogenation of vinylacetylene hydrocarbons, regardless of their structure the triple bond was invariably the most reactive. In other reactions, for example with bromine, there are considerable differences in the reactivity of these hydrocarbons : alkenylacetylenes of type (II) add bromine at the triple bond in the 1,2- and 1,4-position, alkenylacetylenes of type (III) and vinylalkylacetylenes (I) add bromine at the double bond [6]. In the latter case, the reactivity of the double and triple bond, apparently, depends on the direction of the displacement of the electronic plane of the multiple bonds under the effect of radicals. It is possible that a certain increase in the selectivity of hydrogenation in passing from isopropenylacetylene to propenylacetylene may be connected with this phenomenon of electron displacement towards the acetylene group.

EXPERIMENTAL

Propenyl- and butenylacetylenes were prepared from the corresponding alkylpropargylcarbinols [7]. The latter in their turn were prepared from propargyl bromide and the corresponding aldehydes by the Reformatsky reaction [8].

For the work, we used propenylacetylene with b.p. 46.5–47.5°, d_4^{20} 0.7293, n_D^{20} 1.4348; butenylacetylene with b.p. 72–74°, d_4^{20} 0.7425, n_D^{20} 1.4381.

Literature data for propenylacetylene [7]: b.p. 46–48°, n_D^{19} 1.4356.

Vinylalkylacetylenes and isopropenylacetylene were prepared by the usual method, described in previous reports.

Hydrogenation of Propenylacetylene

a) 5.2 g of propenylacetylene in 70 ml of methanol in the presence of 8 ml of colloidal palladium (containing 1 mg of palladium per 1 ml) was hydrogenated until it had absorbed 1.896 ml of H_2 (18°, 754 mm), which corresponds to 1 mole of H_2 to 1 mole of hydrocarbon.

The reaction products were diluted with water, the hydrocarbons distilled off together with water and alcohol, washed with a saturated solution of $CaCl_2$ and dried over $CaCl_2$. The yield of hydrogenation products was 4.8 g (92% of the hydrocarbon taken for hydrogenation). In all operations, measures were taken to eliminate losses due to volatile hydrocarbons.

The hydrogenation product had : B.p. 40–44°, d_4^{20} 0.6911, n_D^{20} 1.4278.

2.3 g of the product was treated with excess bromine in chloroform. After leaving the reaction mixture overnight (in the dark and at a low temperature) the excess bromine was washed out with a solution of sulfite, the chloroform was distilled off on a column in vacuum and the residue was cooled. From this we isolated 5.5 g of crystalline tetrabromide, about 34% of the amount of the mixture.

On distilling the liquid part, two fractions were obtained: 1st–72–75° (20 mm), d_4^{20} 1.7052, n_D^{20} 1.5145, 1 g.

Found %: Br 71.50. $C_5H_{10}Br_2$. Calculated %: Br 69.49.

2nd–140–145° (10 mm), d_4^{20} 2.3267, n_D^{20} 1.5927, 8.8 g.

Found %: Br 81.75. $C_5H_8Br_4$. Calculated %: Br 82.43. Residue in flask – 2 g.

The crystalline tetrabromide melted at 114° after recrystallization from methanol and did not depress the melting point of authentic piperylene tetrabromide.

b) To determine the rate and the character of the process of the complete hydrogenation, experiments were carried out with smaller amounts of material. The hydrogen was measured every 2 minutes. The results of one of the experiments are given in Table 2 in a shortened form and in the figure (curve 4), where along the ordinate is plotted the amount of hydrogen (in milliliters) absorbed for equal time intervals, plotted along the abscissa.

Hydrogenation of Butenylacetylene

a) 4.1 g of butenylacetylene in 100 ml of methanol in the presence of 10 ml of colloidal palladium was

hydrogenated until it had absorbed 1201 ml of hydrogen (18°, 772 mm), which corresponds to the ratio – hydrocarbon : hydrogen = 1 : 1. The reaction products were treated as usual. The yield was 3.5 g (85%).

B. p. 70–73°, d_4^{20} 0.7071, n_D^{20} 1.4323.

TABLE 2

Time (in minutes)	6	12	18	24	30	36	42	48	54	60
v (in ml)	29	84	146	213	295	440	691	751	775	790
Percentage absorption of hydrogen	2.5	7.2	12.5	13.2	25.2	37.6	59.1	64.3	66.3	67.6

Footnote. 1.089 g of propenylacetylene, 50 ml of methanol, 4 ml of colloidal palladium (1 mg per 1 ml), 18° (768 mm), calculated volume of hydrogen ν (allowing for $3H_2$) 1169 ml.

As a result of bromination of 3.1 g of the hydrogenation products, 2 fractions of bromides were obtained.

1st up to 100° (5 mm), d_4^{20} 1.6333, n_D^{20} 1.5138, 0.9 g.

Found %: Br 68.57, 68.61. $C_6H_{12}Br_2$. Calculated %: Br 65.51.

2nd–140–145° (5 mm), 10.5 g.

Found %: Br 79.85, 79.99. $C_6H_{10}Br_4$. Calculated %: Br 79.56. Residue 1.5 g.

The second fraction partially crystallized on standing. The crystals were separated off the liquid part and washed with cold methanol. The yield was 1.9 g (18% of the amount of mixture). The m.p. was 91.5° (from methanol). A sample mixed with authentic tetrabromide of hexadiene-1,3 melted at the same temperature.

b) Data on the rate of hydrogenation of butenylacetylene are shown in the figure (curve 5). Conditions of the experiment: 0.9224 g of butenylacetylene, 18°, 768 mm, calculated volume of hydrogen ($3H_2$) 817.3 ml.

Hydrogenation of Isopropenylacetylene

a) 8.97 g of isopropenylacetylene in 120 ml of methanol was hydrogenated in the presence of 15 ml of colloidal palladium until it absorbed 3202 ml of hydrogen (15°, 762 mm), which corresponds to the ratio – hydrocarbon : hydrogen = 1 : 1. The yield of hydrogenation products was 7 g (80%).

B.p. 30–33°, d_4^{20} 0.6813, n_D^{20} 1.4130.

On distilling the bromides, prepared from 6.1 g of the hydrogenation products, two fractions were isolated.

1st–55–65° (12 mm), d_4^{20} 1.6830, n_D^{20} 1.5140, 2.9 g.

Found %: Br 69.65, 69.81. $C_5H_{10}Br_2$. Calculated %: Br 69.49.

2nd–145–155° (5 mm), d_4^{20} 2.3570, n_D^{20} 1.6057, 21 g.

Found %: Br 81.83. $C_5H_8Br_4$. Calculated %: Br 82.43. Residue 1.8 g.

2.6 g of the hydrogenation product of isopropenylacetylene was heated with 3.3 g of maleic anhydride in a toluene solution at 120° for 5 hours. Then the greater part of the toluene was distilled off and the residue was heated on a water bath with a twofold excess of 10% sodium hydroxide solution for 5 hours. On acidifying the alkaline solution (to congo red), 4-methyl-Δ4-tetrahydrophthalic acid precipitated. The yield was 5.9 g. The

m.p. was 151–152° (from water), which corresponds to literature data [9].

b) Data on the rate of hydrogenation of isopropenylacetylene is given in Table 3 and in the figure (curve 3).

TABLE 3

Time (in minutes)	6	12	18	24	30	36	42	48	54
v (in ml)	47	139	253	384	611	809	837	845	848
Percentage absorption of hydrogen	3.7	11.0	20.0	30.4	48.5	64.1	66.2	67.0	67.2

Footnote. 1.137 g of isopropenylacetylene, 50 ml of methanol, 4 ml of colloidal palladium; 18° (743 mm), calculated volume of hydrogen v ($3H_2$) 1265 ml.

Hydrogenation of Vinylmethyl- and Vinylethylacetylenes

Data on the rate of hydrogenation and the composition of the hydrogenation products for these hydrocarbons has already been published [1]. In the figure are given new experimental results, obtained with the same sample of catalyst as was used in the case of the other hydrocarbons (curves 1 and 2). They did not differ in principle from the data already published.

SUMMARY

1. The catalytic hydrogenation of propenyl-, isopropenyl- and butenylacetylenes over colloidal palladium was investigated.

2. It was shown that the above monosubstituted acetylenes (alkenylacetylenes) are hydrogenated much more selectively than disubstituted acetylenes – vinylalkylacetylenes, and give a high yield of the corresponding diene hydrocarbons. The selectivity of the process is higher with hydrocarbons of normal structure.

3. A possible explanation is given for this difference in behavior in the catalytic hydrogenation of vinylacetylene hydrocarbons.

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INVESTIGATIONS IN THE FIELD OF DERIVATIVES OF β-DICARBONYL COMPOUNDS

I. SYNTHESIS OF β-CHLOROVINYL KETONES

V. T. Klimko, V. A. Mikhalev and A. P. Skoldinov

β-Dicarbonyl compounds have been widely applied in organic synthesis and, in particular, in the preparation of various heterocyclic compounds. Acylacetaldehydes ($RCOCH_2CHO$ [1, 2]) could be the starting materials for the synthesis of a whole series of heterocyclic compounds containing alkyl or aryl substituents in the nucleus. However, the application of these compounds is limited due to their instability in the free state, relative inaccessibility of higher homologs and low yields when synthesized [2]. As has been shown in a number of papers in the last few years, β-chlorovinyl ketones ($RCOCH{=}CHCl$), which may be considered as chloro derivatives in the enol form of acylacetaldehydes, successfully replace β-acylacetaldehydes in the synthesis of different organic compounds and, furthermore, make possible a whole series of syntheses, which could not be carried out before or only with great difficulty [3]. Due to this, the interest in β-chlorovinyl ketones has greatly increased recently. Usually, the condensation of acid chlorides with acetylene [4] or with vinyl chloride [5], which was more accessible and convenient for laboratory work, in the presence of aluminum chloride was used for the synthesis of β-chlorovinyl ketones. The synthesis of β-chlorovinyl ketones from acetylene was developed in very great detail and perfected by A. N. Nesmeyanov, N. K. Kochetkov et al. [6], its synthesis from vinyl chloride – by the authors of this paper [7].

In carrying out the first experiments on the condensation of acetyl chloride with vinyl chloride in the presence of aluminum chloride in a chloroform medium, we obtained, after steam distilling the reaction mixture and distilling off the solvent, a liquid product which distilled at 74–76° (100 mm), and when stored for twenty-four hours, decomposed with the splitting off of hydrogen chloride and formation of a thick blackish-brown liquid; the chlorine content of this product exceeded that calculated for methyl β-chlorovinyl ketone. As we assumed that the high chlorine content was due to the presence in the product of traces of methyl β,β-dichloroethyl ketone, we decided to undertake the isolation of this compound in a pure state. By decomposing the mixture with ice and rapidly separating the chloroform solution of the reaction products from the water layer, we were able to isolate by subsequent distillation in vacuum pure methyl β,β-dichloroethyl ketone, which up to now had been a hypothetical intermediate product in the synthesis of methyl β-chlorovinyl ketone from vinyl and acetyl chloride [3]. Although this compound decomposed rapidly when stored, it was capable of existing in the free state, contradicting the opinion held by Cotch and co-authors [5]. When heated for several hours with weak bases (chalk, sodium bicarbonate, etc.) in an aqueous medium, methyl β,β-dichloroethyl ketone split off a molecule of hydrogen chloride and was converted into methyl β-chlorovinyl ketone:

$$CH_3COCl + CH_2{=}CHCl \xrightarrow{AlCl_3} CH_3COCH_2CHCl_2$$
$$CH_3COCH_2CHCl_2 \xrightarrow[H_2O]{OH'} CH_3COCH{=}CHCl.$$

The latter, in a pure state, turned out to be more stable and could be stored for several days in the dark without noticeable decomposition. Considering the instability of methyl β,β-dichloroethyl ketone, we did not try to isolate this compound or its homologs as individuals in the following experiments, but worked out a pro-

cedure by which the alkyl β,β-dichloroethyl ketone could be converted into the corresponding β-chlorovinyl ketone without its preliminary separation from the reaction solution. By this method, we obtained the following in yields of 50–84%(of the original acyl halides): methyl, ethyl, propyl, isobutyl and n-amyl β-chlorovinyl ketones.

In carrying out the condensation of vinyl chloride with benzoyl chloride and its derivatives, we discovered that the aryl β,β-dichloroethyl ketones, formed as an intermediate product, are considerably more stable than their aliphatic analogs. Phenyl, p-nitrophenyl and p-methoxyphenyl β,β-dichloroethyl ketones were prepared. The conditions under which the condensation for obtaining the first two compounds was carried out were the same as for the synthesis of compounds of the aliphatic series. The yields were 71 and 67% respectively. We were unable to prepare the corresponding β,β-dichloroethyl aryl ketone by the reaction of p-methoxybenzoyl chloride, with vinyl chloride in the presence of anhydrous aluminum chloride, apparently, due to the methoxyl group becoming involved in the reaction. However, using a solution of anhydrous aluminum chloride in nitromethane [8] as condensing agent, we were able to prepare p-methoxyphenyl β,β-dichloroethyl ketone in a yield more than 60%.

The aryl β,β-dichloroethyl ketones obtained were quite stable when stored and only split off hydrogen chloride very slowly when boiled with aqueous solutions of sodium bicarbonate or carbonate. The aryl β,β-dichloroethyl ketones were converted most readily into the corresponding β-chlorovinyl ketones by reacting the former with trialkylamines, for example, with triethylamine :

$$RCOCH_2CHCl_2 + N(C_2H_5)_3 \longrightarrow RCOCH{=}CHCl + (C_2H_5)_3N \cdot HCl.$$

The splitting off of hydrogen chloride took several minutes after a solution of triethylamine in an organic solvent was added to a solution of the β,β-dichloroethyl ketone in the same solvent. When the order of addition was reversed or when an excess of triethylamine was introduced, besides the splitting off of hydrogen halide, a side reaction occurred: the reaction of β-chlorovinyl ketone with triethylamine to form a quaternary ammonium base.*

Although the second stage of the reaction proceeded more slowly than the first, its rate was sufficient, when a large excess of triethylamine was added, for a quantitative argentometric determination of chlorine in the β,β-dichloroethyl and β-chlorovinyl ketones. This reaction made possible the quantitative determination of the amount of aryl β,β-dichloroethyl ketones in the reaction solutions and made possible the preparation of aryl β-chlorovinyl ketones without the intermediate separation of the dichlorides in the pure state. We used the preparation of o-bromophenyl β-chlorovinyl ketone as the example of this type of synthesis.

EXPERIMENTAL

Methyl-β,β-dichloroethyl ketone. With external cooling and stirring (temperature 10–15°), 66.5 g of anhydrous aluminum chloride was added to a solution of 39 g of acetyle chloride in 50 ml of cholorform. Over a period of 1.5–2 hours vinyl chloride, prepared from 119 g of dichloroethane and potassium hydroxide in aqueous alcohol solution [10], was passed through the mixture at 24–26°, after which stirring was continued for a further 10 minutes. Then the reaction mixture was poured onto crushed ice, the chloroform layer was separated, dried for 2 hours over calcium chloride and quickly distilled in vacuum. We obtained 40 g of a substance (50%, calculated on acetyl chloride). The colorless liquid with a sharp odor liberated hydrogen chloride and on standing for two days was converted into a black, solid, spongy mass.

B.p. 60–62° (8 mm), n_D^{18} 1.4571, d_4^{20} 1.242.
Found %: Cl 50.12. $C_4H_6OCl_2$. Calculated %: Cl 50.35.

Methyl β-chlorovinyl ketone. 24 g of methyl β,β-dichloroethyl ketone was mixed with 10 g of calcium carbonate and 100 ml of water. The mixture was boiled for 2 hours under reflux, cooled, filtered, the methyl β-chlorovinyl ketone extracted with chloroform and the chloroform layer dried and distilled in vacuum. We obtained 12.7 g (67%) of a substance with a solidifying point of 8.7°. On standing for a week out of the light at a

*N. K. Kochetkov and A. Ya. Khorlin obtained salts of trialkylketoalkenylammonium at the same time as we did; therefore, we carried out their isolation and further investigation together [9].

temperature of 12–14°, the substance acquired a brown color, but did not liberate hydrogen chloride and distilled in vacuum without decomposition.

B.p. 40° (15 mm), n_D^{18} 1.4691, d_4^{18} 1.122. Literature data [4]: b.p. 38–39° at 18 mm, n_D^{20} 1.4683.
Found %: Cl 34.10. C_4H_5OCl. Calculated %: Cl 33.97.

Ethyl β-chlorovinyl ketone. A current of vinyl chloride, prepared from 59 g of dichlorethane, was passed through a mixture of 23 g of propionyl chloride, 50 ml of chloroform and 33 g of anhydrous aluminum chloride over a period of 2 hours. After the end of the reaction and the decomposition with ice, the chloroform layer was washed with water and then refluxed with a mixture of 8 g of sodium bicarbonate and 25 ml of water. During the time of heating, every 30 minutes a sample was taken and the chlorine content determined by a Mohr or Volhard titration. The splitting out of hydrogen chloride was considered complete when two subsequent determinations gave the same chlorine content in the aqueous solution (usually after 4–5 hours). The chloroform layer was separated, dried over sodium sulfate and distilled in vacuum. We obtained 15 g (50.7% calculated on the propionyl chloride) of ethyl β-chlorovinyl ketone. It was a colorless liquid.

B.p. 48–51° (15 mm), n_D^{20} 1.4610, d_4^{20} 1.0910. Literature data [6]: b.p. 55–56° (27 mm), n_D^{20} 1.4596, d_4^{20} 1.0702.
Found %: Cl 30.29. C_5H_7OCl. Calculated %: Cl 29.95.

Similarly we prepared:

Methyl β-chlorovinyl ketone (yield 84%).
Propyl β-chlorovinyl ketone (yield 73.5%).

B.p. 57–59° (12 mm), n_D^{20} 1.4620, d_4^{20} 1.0520. Literature data [6]: b.p. 56–57° (12 mm), n_D^{20} 1.4640, d_4^{20} 1.0396.
Found %: Cl 26.90, 26.72. C_6H_9OCl. Calculated %: Cl 26.79.

Isobutyl β-chlorovinyl ketone (yield 65.7%).

B.p. 62–63° (12 mm), n_D^{20} 1.4578, d_4^{20} 1.0124. Literature data [6]: b.p. 64–65° (12 mm), n_D^{20} 1.4590, d_4^{20} 1.0117.
Found %: Cl 24.38, 24.24. $C_7H_{11}OCl$. Calculated %: Cl 24.23.

n-Amyl β-chlorovinyl ketone (yield 59.9%).

B.p. 76–77° (7 mm), n_D^{20} 1.4620, d_4^{20} 1.0157. Literature data [11]: b.p. 87–88° (12 mm), n_D^{20} 1.4615, d_4^{20} 0.9960.
Found %: Cl 22.24, 21.97. $C_8H_{13}OCl$. Calculated %: Cl 22.11.

Phenyl β-chlorovinyl ketone (yield 63.7%).

B.p. 120–123° (10 mm), n_D^{20} 1.5770, d_4^{20} 1.2080. Literature data [12]: b.p. 125–127° (18 mm), n_D^{20} 1.5742.

p-Nitrophenyl β,β-dichloroethyl ketone. Into a solution of 18.5 g of p-nitrobenzoyl chloride in 100 ml of dichloroethane at 20–25° 13.3 g of anhydrous aluminum chloride was gradually introduced over an hour, while at the same time a stream of vinyl chloride, prepared from 15 g of dichloroethane, was passed through. At the end of the addition, the vinyl chloride was passed for a further 1.5–2 hours, while the temperature of the reaction mixture rose on its own to 40–45°. The reaction mixture was poured onto ice, the dichloroethane layer was separated and to remove the unreacted p-nitrobenzoyl chloride, it was boiled under reflux for 2 hours after adding 100 ml of 10% sodium bicarbonate solution. The dichloroethane solution was again separated and dried over calcium chloride, the dichloroethane was distilled off and the residue was recrystallized from benzene. We obtained 16.3 g (65.7%) of p-nitrophenyl β,β-dichloroethyl ketone, which was light yellow needles with m.p. 81°. The substance was readily soluble in most organic solvents.

Found %: Cl 28.45, 28.39. $C_9H_7O_3NCl_2$. Calculated %: Cl 28.62.

p-Nitrophenyl β-chlorovinyl ketone. With stirring a solution of 4.0 g of triethylamine in 20 ml of ether was gradually added over a period of 10 minutes to a solution of 10.0 g of p-nitrophenyl β,β-dichloroethyl ketone in 80 ml of absolute ether, cooled to 10°. The mixture was left for 2 hours, the precipitate of triethylamine hydrochloride filtered off, the ether evaporated off under water pump vacuum and the residue recrystallized from petroleum ether. We obtained 7.5 g (87.8%) of p-nitrophenyl β-chlorovinyl ketone, which was light yellow needles with m.p. 88–89°. Literature data [13]: 88.5–89°.

Found %: Cl 16.58, 16.40; N 6.47, 6.57. $C_9H_6O_3NCl$. Calculated %: Cl 16.70; N 6.58.

p-Methoxyphenyl β,β-dichloroethyl ketone. A solution of 8 g of aluminum chloride in 15 ml of nitromethane was gradually added to a solution of 8.7 g of anisoyl chloride in 100 ml of dichloroethane, while at the same time vinyl chloride, prepared from 49.5 g of dichloroethane was passed through. The reaction mixture was poured onto ice, the dichloroethane layer separated and boiled for 30 minutes with 200 ml of a 2.5% solution of sodium bicarbonate. Again the dichloroethane layer was separated, the dichloroethane distilled off and the residue extracted with petroleum ether. The petroleum ether was distilled off and the residue recrystallized from light petroleum ether. We obtained 5.7 g (48.9%) of the substance. It was colorless prisms with m.p. 58°.

Found %: Cl 30.00, 30.29. $C_{10}H_{10}O_2Cl_2$. Calculated %: Cl 30.15.

p-Methoxyphenyl β-chlorovinyl ketone was prepared from p-methoxyphenyl β,β-dicholoroethyl ketone as above. The yield was 61.2%. It formed colorless prisms (from petroleum ether) with m.p. 50° [13].

Found %: Cl 18.38, 18.18. $C_{10}H_9O_2Cl$. Calculated %: Cl 18.06.

o-Bromophenyl β-chlorovinyl ketone. With stirring a solution of 14.7 g of aluminum chloride in 20 ml of nitromethane was gradually added over a period of 1 hour to a solution of 24.1 g of o-bromobenzoyl chloride in 100 ml of dichloroethane, while a stream of vinyl chloride was passed through the reaction mixture and then it was passed for a further hour, after which, the reaction mixture was poured onto ice. The dichloroethane solution was separated off and dried over calcium chloride and a 1 ml sample was taken, dissolved in 5 ml of ether and added to 2 ml of triethylamine. After 4 hours the sample was diluted with 59 ml of water, acidified with 2 N nitric acid and a Volhard titration carried out for chlorine (1 ml of 0.1 N silver nitrate solution corresponded to 0.0145 g of o-bromophenyl β,β-dichloroethyl ketone). The calculated yield of o-bromophenyl β,β-dicholoroethyl ketone was 14 g (45.3%). The dichloroethane was distilled off. The residue was dissolved in 100 ml of absolute ether and 5 g of triethylamine was added to it. After 2 hours the precipitate of triethylamine hydrochloride was filtered off, the ether distilled off and the residue treated as in previous experiments. We obtained 11.5 g (42.9% calculated on o-bromobenzoyl chloride) of o-bromophenyl β-chlorovinyl ketone as colorless fine prisms (from petroleum ether) with m.p. 50° [13].

SUMMARY

1. A method has been perfected for the preparation of β-chlorovinyl ketones by the condensation of acid chlorides of carboxylic acids with vinyl chloride and the application of this synthesis has been enlarged.

2. The intermediate products of this synthesis – β,β-dichloroethyl ketones have been isolated and characterized for the first time.

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*T.p = C. B. Translation pagination.

** See C. B. Translation.

MYRCENE MONOXIDE IN GRIGNARD SYNTHESIS

G. V. Pigulevsky and N. A. Adrova

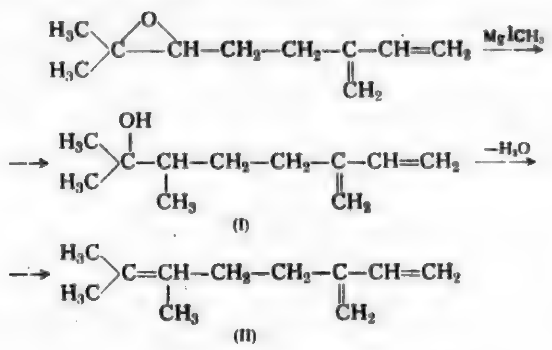
We recently showed [1, 2] that due to the different reactivity of the double bonds it is possible to synthesize myrcene monoxide and dioxide. In this paper we describe the products of the reaction of methylmagnesium iodide with myrcene monoxide.

The formation of the corresponding tertiary alcohol was to be expected in the normal course of the reaction; however, we were able to isolate only a hydrocarbon with the composition $C_{11}H_{18}$ as a result of this reaction. Apparently, an alcohol was also formed; however, as a result of rapid polymerization, a large portion of the product turned brown and was converted into a tar-like mass. We ascribed the structure 2,3-dimethyl-6-methylenoctadiene-2,7 (II) to the myrcene homolog synthesized.

Two lines with the frequencies $\Delta\nu$ 1636 and 1674 cm^{-1} were present in the combination scattering spectrum. The line with the frequency $\Delta\nu$ 1636 cm^{-1} which was quite intense, we considered was due to the conjugated system of double bonds, in analogy with myrcene [2]. As for the line with the frequency $\Delta\nu$ 1674 cm^{-1}, it is characteristic [3] of a secondary-tertiary double bond and is somewhat higher * than that of a tertiary-tertiary double bond.

The higher frequency of $\Delta\nu$ could be explained in our case as due to the effect of the methyl group. Actually, lines with somewhat higher frequencies, $\Delta\nu$ 1679 and 1676 cm^{-1}, are characteristic of trimethylethylene and tetramethylethylene [4].

The presence of the isopropylidene group in the hydrocarbon synthesized by us was confirmed by the production of large amounts of acetone (0.76 mole) on ozonolysis. Apparently, the hydrocarbon $C_{11}H_{18}$ was formed as a result of the dehydration of alcohol (I) synthesized in the Grignard reaction.



(I)

(II)

To elucidate the behavior of myrcene monoxide in a Grignard reaction, we decided to carry out the same reaction with the saturated monoxide, since under these conditions we considered that the effect of the conjugated system of double bonds would be eliminated. We hydrogenated the monoxide in the presence of platinum black. Tetrahydromyrcene oxide when treated with methylmagnesium iodide gave mainly an unsaturated hydrocarbon

*A line with a frequency of $\Delta\nu$ 1,666 cm^{-1} is characteristic of a tertiary-tertiary double bond.

$C_{11}H_{22}$. Apparently, the anomalous procedure of the Grignard reaction was not due to the conjugated system. A more thorough study of the problem that we have touched upon would, without doubt, clarify the mechanism of the reaction.

EXPERIMENTAL

The reaction of myrcene monoxide with methylmagnesium iodide. The myrcene monoxide was synthesized from myrcene, prepared by the dehydration of linalool. Another sample of myrcene, which was used for the synthesis of the monoxide, was isolated from rosemary oil (Ledum palustre). It gave the same results as the myrcene from the linalool.

An ether solution of methylmagnesium iodide was added in small portions to 100 g of myrcene monoxide, dissolved in 1.5 liters of ethyl ether. Despite the fact that the reaction was carried out with cooling, the solution heated up strongly. Then the reaction mixture was treated with dilute hydrochloric acid with cooling. The ether was distilled off from the dried ether solution and the residue was distilled in vacuum. The 1st fraction distilled at 49–50° (6 mm). On further raising the temperature, the residue in the flask foamed up vigorously, quickly turned brown and polymerized. As a result of this, we used a higher vacuum in a subsequent experiment. However, in this case the residue in the flask amounted to 57% of the myrcene monoxide used in the reaction. On distilling, we obtained the following fractions: 1st-44° (4mm), 35 g; 2nd-50–68° (0.1 mm) 8 g; residue 57 g.

In the 2nd fraction was found 50% of alcohols by the Chugaev – Tserevetinov method. An attempt to isolate the alcohols by means of the borates did not give positive results.

The 1st fraction corresponded to 2,3-dimethyl-6-methylen-octadiene-2,7: d_4^{20} 0.8095, n_D^{20} 1.4740, MR_D 52.08. $C_{11}H_{18}F_3$. calc. 51.50.

Found %: C 87.69, 88.28; H 11.87, 11.96. M 147.1, 144.3. $C_{11}H_{18}$. Calculated %: C 88.00; H 12.00. M 150.

Combination light scattering spectrum of the hydrocarbon $C_{11}H_{18}$: $\Delta\nu$: 692 (1), 805 (1), 905 (1), 1062 (1), 1105 (1), 1151 (1), 1206 (1), 1236 (1), 1294 (4), 1328 (2), 1379 (1), 1414 (1), 1460 (1), 1636 (10), 1674 (4), 2777 (2), 2848 (1), 2924 (1).

For ozonization of the hydrocarbon $C_{11}H_{18}$, we used 5 g of the substance in 50 ml of chloroform. The ozonization was continued until the ozonized substance no longer decolorized bromine water. The chloroform was distilled off in vacuum and the ozonide decomposed by boiling with 50 ml of water for 3 hours. Then 3 ml of 5% hydrogen peroxide was added and the reaction mixture again boiled for 1 hour. To remove the excess hydrogen peroxide, the solution was heated with platinum gauze until it gave a negative reaction with KI. After neutralization with soda, the solution was distilled. In all we obtained 64 ml of distillate, in which the acetone was determined by Messinger's method. From 1 mole of hydrocarbon we obtained 0.76 mole of acetone.

For the catalytic hydrogenation of myrcene monoxide, we used 20 g of myrcene monoxide and 2 g of platinum. The amount of hydrogen, sufficient to saturate two double bonds was 5895 ml (0°, 780 mm), In the hydrogenation, 5600 ml of hydrogen was used. After distilling the hydrogenation products, 17 g of tetrahydromyrcene monoxide was isolated.

B.p. 65–66° (23 mm), d_4^{20} 0.8321, n_D^{20} 1.4278, MR_D 48.21; calc. 47.82.
Found %: C 77.02, 77.13; H 12.81, 12.96. $C_{10}H_{20}O$. Calculated %: C 76.92; H 12.82.

Combination light scattering. $\Delta\nu$: 229 (1), 309 (1), 367 (1), 446 (1), 454 (1), 680 (4), 738–753 (1), 798–823 (1), 861 (1), 913 (1), 969 (1), 1041 (1 broad), 1098 (1), 1140 (1), 1192 (1), 1245 (0), 1317 (1), 1377 (1), 1422-1461 (2), 2917 (4 broad), 2964 (4 broad).

The reaction of tetrahydromyrcene monoxide with methylmagnesium iodide. An ether solution of methylmagnesium iodide was added to an ether solution of hydrogenated myrcene monoxide (35 g). The reaction conditions were the same as in the case of myrcene monoxide. In contrast to the latter, the reaction did not heat up noticeably. The reaction products were distilled in vacuum; this yielded the following fractions: 1st-40–42° (14 mm), 10 g, 2nd- 40–42° (0.2 mm), 5 g of colored product.

The 1st fraction apparently corresponded to 2,3,6-trimethyloctene-2: d_4^{20} 0.7640, n_D^{20} 1.4360, MR_D 52.69. $C_{11}H_{22}F$. calc. 52.53.
Found %: 85.37, 85.54; H 14.62, 14.37. $C_{11}H_{22}$. Calculated %: C 85.71; H 14.28.

SUMMARY

The reaction of myrcene monoxide with methylmagnesium iodide gave a hydrocarbon $C_{11}H_{18}$, with structure of 2,3-dimethyl-6-methylen-octadiene-2,7.

The reaction of tetrahydromyrcene monoxide with methylmagnesium iodide gave a hydrocarbon $C_{11}H_{22}$.

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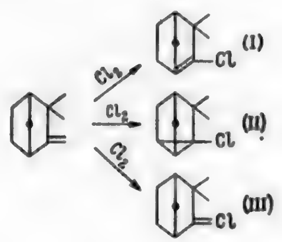
A NEW TYPE OF TERPENE REACTION

XVII. THE ACTION OF CHLORINE ON ω-CHLOROCAMPHENE

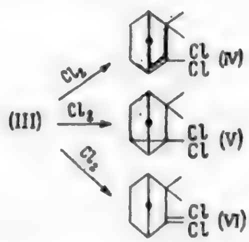
D. Tishchenko and T. Prokhorchuk

It was shown earlier that in the reaction of chlorine with camphene the "anomalous" reaction of M. D. Lvov had, in comparison with other terpenes, the smallest relative weight (~50), and that three chloroterpenes and 2,10-dichlorocamphane were produced [1, 2].

Bredt's prohibition hinders the course of the "anomalous" reaction, therefore, besides the expected chloroterpene (I), two others, (II) and (III), are formed:



If our hypotheses on the mechanism of M. D. Lvov's reaction are correct, then the relative weight of the "anomalous" reaction should be higher in the chlorination of ω-chlorocamphene than in the case of camphene, as the negative inductive action of the chlorine atom would strengthen the polarization necessary for the anomalous reaction of the double bond. Furthermore, it was necessary to find out whether dichloroterpene (IV), a homolog of (I), would be formed by this reaction with the breakdown of Bredt's prohibition:



The purpose of this paper was to clarify these questions. The first hypothesis was confirmed: the "anomalous" reaction proceeded with a yield of not less than 63%. In the mixture of dichloroterpenes 39% of the total content isolated was saponifiable chlorine. As the acetate of the enol of chlorocamphenylane aldehyde (see below) was formed by the reaction of the dichloride (IV) with potassium acetate, then

(IV) 

the content of (IV) in the mixture was not less than 78%. The calculated amount of acetic acid and chloroaldehyde were obtained by saponifying the ester of the chloroenol. The nonlability of the chlorine atom in the chloroenol ester and in the chloroaldehyde was due to its situation at the head of the bridge [3]. The structure of (IV) was not definitely proved but seems extremely probable on the basis of the reactions described.

EXPERIMENTAL

For the chlorination we used the inert chloride of camphene, containing not less than 80% of (III), prepared earlier by chlorinating camphene [1]. The substance (II) did not react with chlorine under the reaction conditions we chose. Constants of the chloride: d_4^{20} 1.025, n_D^{20} 1.4985. The chlorination was carried out under the conditions described earlier [1] The percent of "anomalous" reaction was 63.3 in one experiment and 69.5 in another. A liquid fraction of the dichlorides (b.p. 110–112° at 12 mm) was obtained by distilling the reaction product. For it we found:

d_4^{20} 1.156, n_D^{20} 1.5124, MR_D 53.25; calc. 53.25.
Found %: C 58.2; H 7.4; Cl 32.5, 32.5. $C_{10}H_{14}Cl_2$. Calculated %: C 58.5; H 6.9; Cl 34.6.

The dichloride contained small traces of monochloride. On boiling, a sample of the dichloride with a solution of potassium acetate in acetic acid for 12 hours, 39.2% of the chlorine in the sample was mineralized.

Preparation of the chloroenol ester. A sample of the dichloride was boiled (12 hours) with excess potassium acetate in acetic acid, then the solution was diluted with three volumes of water and extracted with petroleum ether, the ether evaporated off from the extract and the residue distilled. We obtained the dichloride with traces of the enol ester (% Cl 26;6) and the acetic ester of the chloroenol with b.p. 116° at 3 mm.

d_4^{20} 1.114, n_D^{20} 1.4933, MR_D 59.61; calc. 59.27.
Found %: Cl 15.6, 15.8. $C_{10}H_{14}ClOCOCH_3$. Calculated %: Cl 15.5.

The substance decolorized bromine water and permanganate solution.

Saponification of the chloroenol ester. 2.3 g was boiled for 3 hours with 100 ml of 1% H_2SO_4 (reflux condenser) and then the volatile acids were distilled off in steam until the distillate was neutral. The distillate was titrated with normal alkali; 71.6 ml was used up, the calculated amount was 71.1 ml. The neutral substances were extracted from the distillate and the neutralized residue with ether and the ether was evaporated off from the extract. The residue gave a qualitative aldehyde reaction.

Found %: Cl 16.9. $C_{10}H_{15}OCl$. Calculated %: Cl 19.0.

SUMMARY

1. In the chlorination of ω-chlorocamphene, according to our hypotheses on the mechanism of Lvov's reaction, the "anomalous" reaction must have a greater relative weight than in the case of camphene and this was proved to be so.

2. The presence in the mixture of unsaturated dichlorides of camphene, the dichloride (IV) and bicyclo-[1,2,2]-3-dichloromethyl-2,2-dimethylheptene-3, formed with the breakdown of Bredt's prohibition, was established with a high degree of probability.

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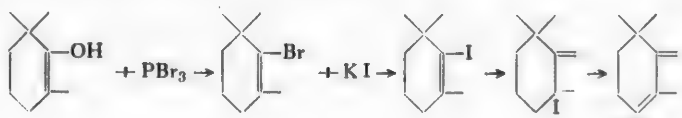
THE STRUCTURE OF PYRONENES

D. Tishchenko and N. Summ

B. A. Arbuzov discovered the thermal isomerization of α-pinene in alloocimene and dipentene [1], Dupont and Dulou isolated two new terpenes, named α- and β-pyronenes from this isomerizate [2]. Later on, Goldblatt and Palkin showed that the pyronenes were formed as a result of the cyclization of alloocimene [3]. Dupont and Dulou found that these pyronenes had the carbon skeleton of 1,1,2,3-tetramethylcyclohexane and suggested for α-pyronene the structure 1,1,2,3-tetramethylcyclohexadiene-3,5 (I) and for β-pyronene – 1,1,2,3-tetramethylcyclohexadiene 2,4 (II), based on the following facts that they obtained: both terpenes condensed with maleic anhydride and with the dimethyl ester of acetylene dicarboxylic acid (the presence of a system of conjugated double bonds); by hydrogenating (I) and (II) hydrocarbons were obtained which had absorption spectra, similar to those of synthetic 1,1,2,3-tetramethylcyclohexane; the product of condensation of (I) with acetylene dicarboxylic ester, on pyrolysis, gave a mixture of isobutylene, trimethylethylene and the dimethyl ester of 3-methyl-o-phthalic acid, while the corresponding products of (II) were isobutylene and the ester of 3,4-dimethyl-o-phthalic acid; condensation products were obtained with acrolein and α-naphthoquinone. Up to now these structural formulas for (I) and (II) have been accepted generally and have not been questioned.

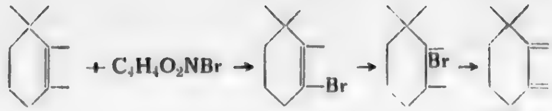
Later on, [4], Dupont named a hydrocarbon, obtained earlier by Kuhn [5], γ-pyronene and "confirmed" the structure suggested by Kuhn – 1,1,3-trimethyl-2-methylencyclohexene-3 (III). Kuhn based his idea on one of the isomers of cyclogeraniol, to which he ascribed, with no proof, the structure 1,1,3-trimethyl-2-methylocyclohexene-2. He converted this alcohol into the bromide (structure undetermined) by treatment with phosphorus tribromide in the presence of a small amount of pyridine and he obtained a hydrocarbon, with a great deal of iodine (reduction !), from the bromide by the action of potassium iodide in boiling acetone. According to Kuhn, these reactions may be expressed by the following formulas:



(III)

According to Kuhn's data, this hydrocarbon contains 0.35 % less carbon and 0.50% more hydrogen than $C_{10}H_{16}$, while its molecular refraction exceeds the value calculated for (III) by only 0.29. Dupont repeated Kuhn's synthesis, determined the boiling point and specific gravity of the hydrocarbon, took the combination scattering spectrum and found the low frequencies of the double bonds; he noted the impossibility of condensing it with maleic anhydride and showed that the hydrocarbon was converted at 500° into m-xylene. Having obtained this information, he considered Kuhn's formula (III) "confirmed."

In the same article [4] Dupont described the preparation of a fourth pyronene, δ-pyronene, by the action of bromosuccinimide on cyclogeraniolene and the removal of hydrogen bromide from the bromide by heating with dimethylaniline. According to Dupont, these reactions should be expressed in the following way:



(IV)

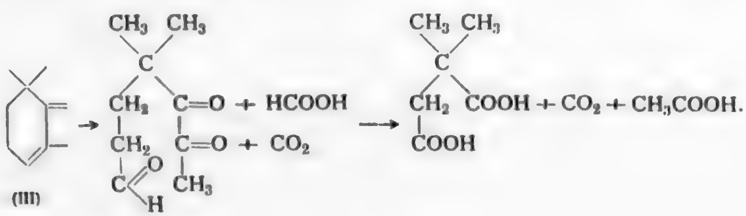
For the hydrocarbon fraction obtained, Dupont determined the specific gravity (0.851, the temperature was not given) and refractive index (n^{18} 1.471, the wave length was not given), he discovered the low frequencies of the double bonds in the combination scattering spectrum and noted the formation of formic acid by ozonolysis (the amount was not given and other products were not investigated). This information Dupont considered sufficient for ascribing structure (IV) to the "δ-pyronene." If we assume that the refractive index was determined for the yellow sodium line and calculated the molecular refraction, we obtain a negative value −0.56(!), which is most extraordinary for a conjugated diene (IV). The qualitative discovery of formic acid in the ozonolysis products (IV) has no bearing on the establishment of the hydrocarbon's structure. It is generally known that it is obtained in small amounts by the action of ozone on saturated compounds as well.

It follows from the above that the "γ- and δ-pyronenes" were not obtained in the pure state, while formulas (III) and (IV) suggested for them, have no foundation and are given, mainly, on the basis of "the principle of least structural change in chemical reactions" and on the arbitrary interpretation of the frequencies of combination scattering spectra.

Dupont hardly gave a firmer basis for the structural formulas suggested by him for α- and β-pyronenes (I and II). He did not apply oxidation or ozonolysis for this purpose, but pyrolyzed the products of the addition of acetylene dicarboxylic ester to α- and β-pyronene. Apparently, it was accepted that condensation was possible in the case of a cis-conjugated system and was impossible in the case of a trans-system ("γ-pyronene"), but the possibility of regrouping of double bonds from the trans- into the cis-position during condensation was not taken into account (for example, abietic acid — levopimaric acid). Pyrolysis cannot be considered a smooth method of simplifying organic materials that never causes any isomerization. Therefore, we believe that none of the structural formulas suggested for the four pyronenes have sufficient basis and the so-called γ- and δ-pyronenes are not separate substances.

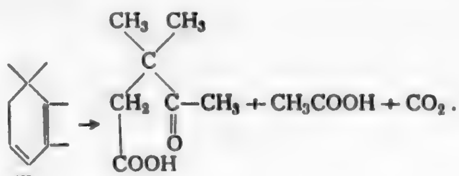
We considered it necessary to establish the structure of β-pyronene so as to be able to investigate some of its reactions, and for this purpose we carried out the ozonolysis of 20 g of this terpene and the oxidation of 50 g with potassium permanganate in an acetone solution. The oxidation gave the clearest results with a consumption of 7.5 g-at. of active oxygen.

More than 20 g of γ,γ-dimethyl-δ,ϵ-diketocaproaldehyde, 8 g of the corresponding acid, 10 g acetic acid, 2 g formic acid, a large amount of carbon dioxide, 3 g dimethylsuccinic acid and 4.5 g α,α-dimethyllevulinic acid were obtained. Examination of the possible oxidation products of eight isomers of the composition $C_{10}H_{16}$ with the skeleton 1,1,2,3-tetramethylcyclohexane showed that the first two materials (28 g) could be formed only from a hydrocarbon of structure (III):



(III)

α,α-Dimethyllevulinic acid could be formed only from a hydrocarbon of structure (II) (Dupont's "β-pyronene"):



(II)

Further oxidation of γ,γ-dimethyl-δ,ϵ-diketocaproic acid should give α,α-dimethylglutaric acid and then α,α-dimethylsuccinic acid, as described in the literature [6]. The formation of dimethylsuccinic acid by the oxidation of dimethyllevulinic acid is improbable as it would contradict Popov's law.

These data make it clear that the β-pyronene oxidized was a mixture of at least 80% of isomer (III) (Dupont's "γ-pyronene") and not more than 20% of isomer (II) (Dupont's "β-pyronene").

The ozonolysis gave the same results. Formaldehyde and formic acid (together about 1/3 g mole), acetic acid (about 1.0 g mole), a diketoaldehyde $C_9H_{14}O_3$, and the acid $C_9H_{14}O_4$ were obtained. Methylglyoxal and dimethyllevulinic aldehyde $C_7H_{12}O_2$ were not obtained. All these materials may be obtained simultaneously only by ozonolysis of a hydrocarbon with structure (III). Dimethyllevulinic aldehyde was not isolated, apparently, as we had ozonized 20 g and oxidized 50 g of the hydrocarbon.

Consequently, β-pyronene is not Dupont's "β-pyronene" and all the ideas of this author are refuted: γ-pyronene has not been studied properly, and the authenticity of the structural formulas proposed by Dupont for α- and δ-pyronenes becomes even more questionable. This example illustrates clearly the unreliability of structural formulas proposed on the basis of reactions that include isomerization phenomena, some qualitative reactions, and the uncritical application of physical methods of investigation .

EXPERIMENTAL

Oxidation of β-pyronene. β-Pyronene was prepared by thermal isomerization of alloocimene. The isomerizate was distilled on a column with an efficiency of about 20 theoretical plates at a pressure of 20 mm and a reflux ratio of 12–15. We collected the fraction with b.p. 63–64°, d_4^{20} 0.847, n_D^{20} 1.4807.

Into a round-bottomed flask was placed 50 g of the terpene and 50 ml of water. With cooling and stirring, a solution of 290 g of $KMnO_4$ in 2 liters of acetone was added dropwise. Towards the end, the decolorization slowed down and the bath was heated to 50°. The manganese dioxide was sucked dry, ground up, extracted with 1 liter of acetone, the acetone sucked off and the operation repeated. The acetone was distilled off from the acetone filtrates (5 liters) with a column and the residue extracted three times with 0.5 liter of ether. The ether was evaporated off from the extracts and the neutral substances were in the residue. The residue almost completely (20 g) distilled at 125–127° and 14 mm. The distillate in the receiver crystallized. After one recrystallization from petroleum ether the substance melted at 69–70° and subsequent recrystallizations did not change the melting point. It was readily soluble in alcohol, ether and benzene, volatile in steam, was not titrated by alkali in the cold and on boiling (not a lactone), did not give a color with ferric chloride (not an enol) and reduced silver reagent (aldehyde group).

Found %: C 63.8, 63.5; H 8.4, 8.2. $C_9H_{14}O_3$. Calculated %: C 63.5; H 8.2.

The monosemicarbazone of the diketoaldehyde was prepared by the usual method in an aqueous alcohol solution, m.p. 208°.

Found %: C 52.7; H 7.6; N 19.2. $C_{10}H_{17}O_3N_3$. Calculated %: C 52.8; H. 7.5; N 18.5.

Oxidation of the diketoaldehyde. 0.5 g of the substance, 25 ml of alcohol, 60 ml of 0.1 N sodium hydroxide and 15 ml of 20% hydrogen peroxide was refluxed for 1 hour and then the solution was diluted twofold with water and extracted with ether. From the ether extract we obtained 0.25 g of the starting material. The aqueous solution was acidified to congo, and steam distilled until the distillate was neutral. In the distillate, acetic acid was found as the silver salt and this indicated that the diketoaldehyde had the terminal group $CH_3-CO-CO-$ [7].

The acid part of the oxidation products of β-pyronene. After extraction with acetone (see above), the manganese dioxide was extracted three times with boiling water. The aqueous filtrates (3 liters) were combined with the part of the acetone-water solution, which was insoluble in ether (salts, see above), evaporated to 500 ml, acidified to congo with hydrochloric acid (copious evolution of carbon dioxide) and steam distilled until the distillate was neutral. The amounts of formic and acetic acid given above were found in the distillate by the usual method. The residue from the steam distillation was evaporated to dryness in vacuum and extracted with ether. We extracted 31 g of a viscous liquid which distilled at ~ 1.10^{-3} mm. We obtained: 1st fraction (bath temperature 120–150°), 11.5 g, equiv. 128; 2nd fraction (150–220°), 9.0 g, equiv. 177; 3rd fraction (220°), 1.0 g, equiv.

192. From the first fraction was prepared a silver salt with 59.1% silver, which corresponded to the silver salt of dimethylsuccinic acid (60%). As the equivalent of dimethylsuccinic acid is 73, there must have been present in the first fraction a monobasic acid with a molecular weight greater than 128. In a small sample we found that an aqueous solution of the 1st fraction gave a precipitate with semicarbazide acetate. 10.2 g of the 1st fraction was dissolved in 50 ml of water and a solution of 20 g of semicarbazide hydrochloride and 24 g of sodium acetate in 100 ml of water was added. After standing overnight, the solution was filtered, the precipitate washed with water, dried (6.5 g, corresponding to 4.6 g of dimethyllevulinic acid) and recrystallized from alcohol to constant melting point 193° [6].

Found %: C 47.4, 47.7; H 7.7, 7.7; N 21.1. Semicarbazone of dimethyllevulinic acid $C_8H_{15}O_3N_3$. Calculated %: C 47.7; H 7.5; N 20.9.

Examination of the 2nd fraction.

Found %: C 58.2, 57.8; H 7.7, 7.9. Equiv. 176. $C_9H_{14}O_4$. Calculated %: C 58.1; H 7.5. Equiv. 186.

The substance gave an iodoform test. It was oxidized by Semmler and Wallach's method with hypobromite solution [8]. After several hours standing, the solution was acidified to congo and extracted with ether, the ether distilled off from the extract, the residue dried in vacuum and the equivalent determined. Four oxidations of the same sample gradually lowered the equivalent from 176 to 94 (176, 132, 124, 103, 94). The acid with equivalent 103 was neutralized and precipitated with the calculated amount of $AgNO_3$. The precipitate was recrystallized from boiling water, dried and analyzed.

Found %: C 23.3, 23.4; H 3.4, 3.1; Ag 56.5. $C_7H_{10}O_4Ag_2$. Calculated %: C 22.5; H 2.7; Ag 58.0.

The same was done for the silver salt from the acid with equivalent 94.

Found %: C 20.9; H 3.1; Ag 58.9. $C_6H_8O_4Ag_2$. Calculated %: C 20.0; H 2.2; Ag 60.0.

Ozonization of β-pyronene. 236 liters of 5% ozone (calculated 196 liters) was passed into a solution of 20 g of the terpene in 100 ml of chloroform, while it was cooled to −20°. The solution of the ozonide was decomposed by introducing it dropwise into boiling water while the volatile products were trapped. The chloroform layer of the distillate was separated and the chloroform evaporated off. The residue (2.8 g) distilled almost completely at 89–94° (2 mm); d_4^{20} 1.06, n_D^{20} 1.4572.

Found %: C 61.5, 61.9; H 8.9, 8.7. $C_9H_{14}O_3$. Calculated %: C 63.5; H 8.2.

We prepared a semicarbazone with m.p. 208° (after recrystallization from alcohol), which did not depress the melting point of the semicarbazone of dimethyldiketocaproaldehyde (see above). In the aqueous layer we found formaldehyde (0.54 g, determined with dimedone), formic acid (1.47 g, determined by Scales method) and acetic acid (12.1 g, as the silver salt). The ozonolysis products, involatile in steam, were completely soluble in water. The water was distilled off in vacuum and the weight of the viscous residue was 14 g. It was distilled at 0.1 mm on a boiling water bath, when 5.0 g distilled at 80–90° and the residue was 6.5 g. The equivalent of the residue was 190 and for $C_9H_{14}O_4$ it was 186. A sample of the residue (1.8 g) was neutralized with soda and to it was added a solution of 18 g $AgNO_3$, 30 g of NaOH, 65 ml of NH_3 (28%) and 1500 ml of H_2O. It was heated on a boiling water bath until the solution became completely clear. It was worked up in the usual way. We isolated 1.6 g of an acid as a very viscous liquid.

Found %: C 52.6, 52.2; H 7.5, 7.5. $C_7H_{12}O_4$ (dimethylglutaric acid) Calculated %: C 52.5; H 7.5.

1 g of $C_7H_{12}O_4$ was oxidized with 20 ml of nitric acid (d 1.20) until nitrogen oxides were no longer evolved. We obtained 0.9 g of a crystalline acid, which was recrystallized from a mixture of benzene and ligroin. The m.p. was 136–139° and the equiv. 74. For asymmetric dimethylsuccinic acid the equiv. is 73 and the m.p. 137 to 142°.

SUMMARY

1. The reliability of proposed structural formulas for pyronenes was examined. It was shown that not one of them has sufficient basis.

2. The ozonolysis and potassium permanganate oxidation of β-pyronene was carried cut. It was found that it was a mixture of more than 80% of 1,1,3-trimethyl-2-methylencyclohexene-3 (Dupont's "γ-pyronene") and less than 20% of 1,1,2,3-tetramethylcyclohexadiene-2,4 (Dupont's "β-pyronene").

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α-OXIDES OF ALKYFURYL ALCOHOLS

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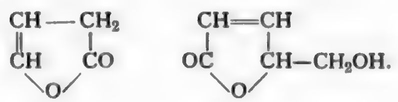
The oxidation of unsaturated alcohols of the aliphatic and aliphatic-aromatic series with peracids for synthesizing α,β-alcohol oxides has been studied quite well [1–4]. The oxidation of alcohols with two double bonds in a molecule has been studied much less, although interesting compounds could be prepared thus.

N. A. Prilezhaev [1, 5] carried out the oxidation of geraniol and linalool with perbenzoic acid and showed that depending on the amount of oxidant either mono- or dioxides of these alcohols could be obtained.

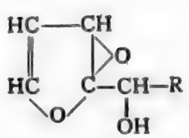
As alcohol oxides of different structure vary a great deal in their properties [3–6], it seemed interesting to us to synthesize alcohol oxides containing a furan ring in the molecule, that is, in particular, α-oxides of alkylfuryl alcohols.

The first example of a compound of this series – furyl alcohol – was oxidized by Boeseken [7] with two moles of peracetic acid. From the reaction products he isolated a small amount of dihydrofuranone-2 (I) and a lactone (II) and up to 80% tar:



(I) (II)

In the present work we carried out the oxidation of ethylfuryl, n-propylfuryl, n-butylfuryl and isoamylfuryl alcohols with acetyl peroxide with molecular ratios of alcohol and peroxide. Under the conditions selected by us, the oxidation products of the alkylfuryl alcohols turned out to be the monoxides of these alcohols: 2-(1-hydroxypropyl)-oxido-2,3-furan (III), 2-(1-hydroxybutyl)-oxido-2,3-furan (IV), 2-(1-hydroxyamyl)-oxido-2,3-furan (V) and 2-(4-methyl-1-hydroxyamyl)-oxido-2,3-furan (VI):

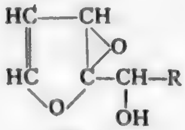


(III) $R = C_2H_5$; (IV) $R = n\text{-}C_3H_7$; (V) $R = n\text{-}C_4H_9$; (VI) $R = iso\text{-}C_5H_{11}$.

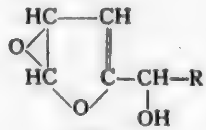
The monoxides (III - VI) are colorless, crystalline materials, dissolving in organic solvents and in water. Their solubility in organic solvents increases with increase in molecular weight, while in water it decreases in the same order. The monoxides of alkylfuryl alcohols obtained by us are unstable materials – when stored in air and even in a desiccator they quite rapidly decompose and are converted into thick, oily liquids with an acrid smell. Their stability increases with molecular weight.

The alcohol oxides (III - IV) reacted with alcohols, amines and water, but the products thus formed were unstable, during the reaction they condensed, forming a tar-like material. The reaction products could not be isolated in a pure state. One of the products of the decomposition of the n-butylfuryl alcohol oxide (V) when

treated with anhydrous zinc chloride turned out to be n- valeraldehyde, which we determined as its condensation product with dimedone. n-Valeraldehyde could have formed, doubtless , due to the splitting off of the side chain from the molecule of butylfuryl alcohol oxide (V). The possibility is not excluded of the preliminary splitting of the furyl ring, as well. The established fact of the splitting off of the side chain from the monoxide (V) with the formation of the aldehyde gave a basis for considering formula (VII) the most probable of the two possible structural formulas for monoxides of alkylfuryl alcohols (VII and VIII) since alcohol oxides which have the alcohol group in an α,β-position to the oxide ring, undergo such decomposition with the formation of aldehydes [2-4, 8-11].



(VII)



(VIII)

EXPERIMENTAL

Preparation of the α-oxide of ethylfuryl alcohol (III). The alcohol was synthesized from ethylmagnesium bromide and furfural. The b.p. was 62.5–63.5° (5 mm). To 13 g of the alcohol in two volumes of anhydrous ether at 20–25° was added 18 g of 90% acetyl peroxide. The reaction proceeded with the evolution of heat. Next day all the peroxide had reacted. The acetic acid was neutralized with soda solution and the ether layer was separated and dried over $MgSO_4$. After distilling off the ether the reaction product was distilled at 7 mm: 1st fraction 75–124°, 2.5 g; 2nd fraction 124–125.5°, 6.5 g; residue 1 g.

The second fraction and the residue quickly crystallized. After two recrystallizations from petroleum ether the substance appeared as fine, colorless needles, readily soluble in water, alcohol, ether and benzene and difficultly soluble in petroleum ether; m.p. 69.5–71°. The yield was 7 g (48%).

Found %: C 59.04; H 6.98; OH 11.80. M 148.1, 147.1. $C_7H_{10}O_3$. Calculated %: C 59.15; H 7.04; OH 11.97. M 142.

The substance obtained corresponded to 2-(1-hydroxypropyl)-oxido-2,3-furan.

Preparation of the α-oxide of n-propylfuryl alcohol (IV). The alcohol was synthesized from n-propylmagnesium bromide and furfural. The b.p. was 92–94° (12 mm).

18.9 g of freshly distilled n-propylfuryl alcohol was oxidized with 10.6 g of 96% acetyl peroxide. The reaction products were treated as in the previous experiment. On distilling the reaction products at 12 mm pressure, the following fractions were obtained: 1st 93–106°; 2nd 106–143°; 3rd 143–145.5° 2.6 g; 4th 145.5°–147° 5.4 g; 5th 147–154°, 2.9 g. The distillation was stopped as decomposition began. The 3rd, 4th and 5th fractions quickly crystallized. After washing these fractions with petroleum ether and recrystallizing twice from a mixture of benzene and petroleum ether (b.p. 19–40°), we obtained a substance with m.p. 57.5–59.5°. The yield was 10.3 g (62.7%). The substance readily dissolved in ether, benzene and carbon tetrachloride, with difficulty in water and was almost insoluble at normal temperatures in petroleum ether. On storing in air, after 2–3 days the melting point changed and then the substance changed into a thick, yeollowish liquid with a sharp smell.

Found %: C 61.44, 61.25; H 8.13, 7.80; OH 10.62. $C_8H_{12}O_3$. Calculated %: C 61.53; H 7.69; OH 10.89.

The substance obtained was 2-(1-hydroxy-n-butyl)-oxido-2,3-furan.

Preparation of the α-oxide of n-butylfuryl alcohol (V). n-Butylfuryl alcohol was synthesized from butylmagnesium bromide and furfural. The b.p. was 85.5–86° (6 mm).

24.5 g of freshly distilled n-butylfuryl alcohol was oxidized with 15 g of 92% acetyl peroxide. The reaction products were treated in the usual way. We obtained a crystalline product, which melted at 82–83° and appeared as short, colorless needles after 2 recrystallizations from benzine (b.p. 80–100°) and from carbon tetrachloride.

The yield was 19.6 g (72.6%). The 2-(1-hydroxyamyl)-oxido-2,3-furan obtained was readily soluble in ether, benzene, alcohol, dichloroethane, dioxane, in benzine on heating and in boiling carbon tetrachloride and was insoluble in water at normal temperature.

Found %: C 63.26; H 8.29; OH 10.13. M 162.3. $C_9H_{14}O_3$. Calculated %: 63.52; OH 10.00. M 270.

Preparation of the α-oxide of isoamylfuryl alcohol (VI). The isoamylfuryl alcohol was synthesized from isoamylmagnesium bromide and furfural and had b.p. 117–118.5° (16 mm).

48 g of freshly distilled isoamylfuryl alcohol was oxidized with 22.5 g of 90% acetyl peroxide. The reaction products were treated in the usual way. Fractions were isolated by distillation at 6 mm: 1st 113–130°, 2 g; 2nd 130–145.5°, 8.2 g; 3rd 145.5–149°, 10.5 g; 4th 149–155°, 15.6 g. The distillation was stopped as decomposition began. The residue was a tarry brown color. The 3rd and 4th fractions were again distilled at 6 mm. We obtained fractions: 1st 134–156°, 7.4 g; 2nd 156–158°, 5 g; 3rd 158–160°, 12.8 g.

The 2nd and 3rd fractions crystallized. After 2 recrystallizations from petroleum ether, we obtained colorless needles with m.p. 60–61.5°. The yield was 15.8 g (30%). The substance was readily soluble in petroleum ether on heating and insoluble in water.

Found %: C 65.08; H 9.09; OH 9.02. M 187.7. $C_{10}H_{16}O_3$. Calculated %: C 65.21; H 8.64; OH 9.23. M 184.

Incompletely purified 2-(4-methyl-1-hydroxyamyl)-oxido-2,3-furan became yellow after several days on storage in air and in a desiccator and deliquesced into a liquid with the smell of rancid butter; the pure oxide was more stable.

Reaction of the oxide of n-butylfuryl alcohol on heating with zinc chloride. A mixture of 3.4 g of the oxide of n-butylfuryl alcohol and 0.8 g of anhydrous zinc chloride was heated for 3 hours on a water bath and then at 150–170°. At this, a liquid with b.p. 95–120° distilled off. The substance gave a product with dimedone, which melted at 105–106° after recrystallization from aqueous alcohol and corresponded to the adduct of dimedone and n-valeraldehyde.

Found %: C 73.13; H 9.34. $C_{21}H_{32}O_4$. Calculated %: C 72.41; H 9.19.

SUMMARY

1. The following four alkylfuryl alcohols were oxidized with acetyl peroxide: ethylfuryl, n-propylfuryl, n-butylfuryl and isoamylfuryl.

2. Four alcohol oxides were obtained and characterized: 2-(1-hydroxypropyl)-oxido-2,3-furan, 2-(1-hydroxybutyl)-oxido-2,3-furan, 2-(1-hydroxyamyl)-oxido-2,3-furan and 2-(4-methyl-1-hydroxyamyl)-oxido-2,3-furan.

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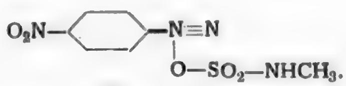
THE REACTION OF DIAZO COMPOUNDS WITH SULFAMIC ACID AND ITS DERIVATIVES

IV. THE DIAZO SALTS OF METHYLARYLTRIAZEN-N-SULFONIC ACIDS

D. Z. Zavelsky and L. A. Lishnevskaya

It was shown in one of our reports [1] that at pH 4–8 potassium N-methylsulfamate condensed with diazo compounds, forming aryl-1-methyl-3-triazensulfonic acids-3. The purpose of this work was to investigate the reaction of potassium methylsufamate with diazo compounds in more acidic media.

The introduction of a concentrated solution of 4-nitrophenyldiazonium chloride into a similar solution of potassium methylsulfamate at a temperature between 2 and 4° and pH 1.0–1.3 gave a yellow precipitate, which had reactions characteristic of diazo salts, but turned out to be heterogeneous when examined microscopically. However, a homogeneous precipitate could be obtained at pH 3, which consisted of light yellow needles that became intense yellow after filtration and drying. Although moderately soluble in water and unstable, the new product could be recrystallized from water acidified with acetic acid by using the difference in the solubilities at 35 and –2°. The recrystallized product consisted of large yellow needles or prisms. Its aqueous solution had a pH of 5.0–5.5 and combined actively with H acid in a neutral medium. This diazo compound was unstable in the dry state as after 2–4 hours it started to show signs of decomposition. When heated, the diazo salt deflagrated, emitting a yellow smoke. After 5–10 minutes in daylight and especially in sunlight, it changed its egg-yellow color to light brown and then to darker brown. The diazo salt that had turned brown after several hours of storage gave an acid reaction and a positive test for sulfate ion when suspended in water, which indicated the splitting out of the sulfo group. Simultaneously, a yellow product, insoluble in water, was formed which turned out to be 4,4'-dinitrodiphenyltriazene. We considered that the material synthesized was the 4-nitrophenyldiazonium salt of methylsulfamic acid (I):



(I)

However, repeated analysis for sulfur, nitrogen and diazo nitrogen content, showed that the material contained much less sulfur and more nitrogen and diazo nitrogen than required by the given formula. Therefore, we considered that the product examined was a molecular compound (II), in which there is 1 mole of the 4-nitrophenyldiazonium salt of methylsulfamic acid per mole of the 4-nitrophenyldiazonium base, as chlorine was not detected in the diazo salt.

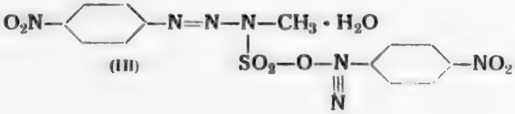
(II)

Actually, the amounts of sulfur, nitrogen and diazo nitrogen calculated for this structural formula agree well with those obtained experimentally as can be seen from Table 1.

TABLE 1

Name of element	Amount of element in %		
	calculated		found
	(I)	(II)	
Sulfur	12.32	7.50	7.39, 7.50
Total nitrogen	21.53	22.94	22.84
Diazo nitrogen	10.77	13.11	13.35

The analysis of the diazo salt for methylsufamic acid by the nitrosation method also confirmed the formula $C_{13}H_{13}O_8N_7S$, however, when combined with m-toluylendiamine or β-naphthol in a neutral medium combination apparently occurred with only 1 mole of the nitrodiazobenzene out of the two contained in the product investigated according to the proposed formula. Therefore, we had to conclude that one of the diazo radicals in the product was in an active and the other in a passive form, and, consequently, structure (III) corresponded to it.

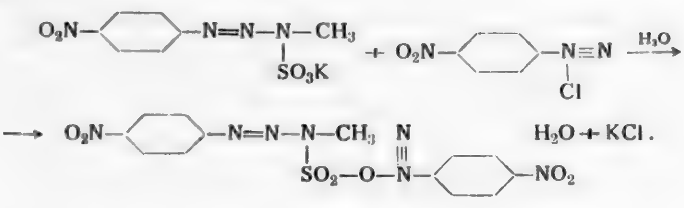


(III)

To check this hypothesis, the material investigated was dissolved in hydrochloric acid in the cold to split the triazene and convert the second diazo group into the active form, and then it was combined with an azo component in a neutral medium. In this case only 79.0–82.0% of both diazo radicals were found, but as the first diazo radical was fixed completely in a separate combination of the product investigated in a neutral medium, only 58–64% of the theoretical amount of the second diazo radical was found to be regenerated from the diazoamino group.

Nitrosation of the methylsulfamic acid in a hydrochloric acid solution of the material before combination, to eliminate secondary formation of the diazoamino compound when neutralized, increased the degree of fixation of the second diazo radical only to 66–67%. Consequently, the second diazo radical could not be fixed quantitatively, under the given analytical conditions, in the form of an azo combination product.

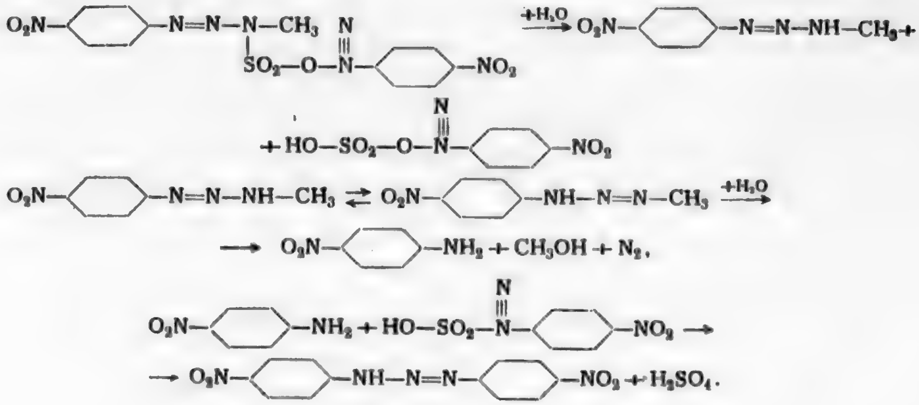
The last formula assumes that the material investigated is the 4-nitrophenyldiazonium salt of (4'-nitrophenyl) -1-methyl-3-triazen-sulfonic acid-3 (III) and, consequently, differs from the potassium salt of this acid, which was synthesized earlier [2], only by a cation. That means that if this formula is correct, salt exchange between 4-nitrophenyldiazonium chloride and the potassium salt of (4'-nitrophenyl)-1-methyl-3-triazensulfonic acid-3 (III) should form a product identical with that obtained from potassium methylsulfamate and two molecules of 4-nitrophenyl diazonium:



Actually, when solutions of nitrophenyldiazonium chloride and the potassium salt of triazensulfonic acid were mixed in the cold, a precipitate was formed whose properties were completely identical with those of the material invesitgated by us. Analysis of the diazoamino diazo salt obtained by the second method for nitrogen and sulfur content further confirmed its similarity to the diazo salt, synthesized by the first method.

Thus, it was established that at pH 3 diazoamino condensation takes place between 4-nitrophenyldiazonium and methylsulfamic acid, but due to the insufficiently high pH and low temperature, it is not complete. The excess diazonium forms a salt of arylmethyltriazen-N-sulfonic acid, analogous to the arylsulfonates of diazo compounds described in the literature [3]. The material is peculiar in that it is simultaneously a diazoamino compound and a diazonium salt.

The formation of sulfate ion and 4,4'-dinitrophenyltriazene by storing an aqueous solution of the diazoamino diazo salt may be readily understood from the following scheme:

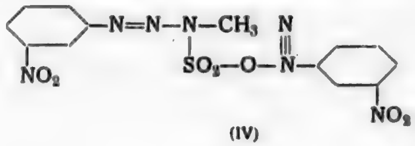


We have already studied thoroughly such a decomposition reaction for potassium salts of various arylmethyltriazen-N-sulfonic acids [4]. The difference, apparently, lies in that hydrolytic splitting of sulfo groups takes place with potassium salt solutions only when heated while with diazonium salts it occurs even in the cold. The lower basicity of the diazo cation in comparison with the potassium cation is, apparently, the reason for this phenomenon.

The reaction which was investigated by using 4-nitrophenyldiazonium, was also applied to other diazo compounds.

A solution of 3-nitrophenyldiazonium chloride combined with a solution of potassium methylsulfamate at —2° and pH 1.5–1.6 to deposit a diazoamino diazo salt, which was similar in properties to that synthesized from 4-nitrophenyldiazonium. Under a microscope it was pale yellow, elongated flat quadrangular plates, which were even less soluble in water than the 4-nitro analog, and therefore, it could not be recrystallized. But when only the middle fractions of the crystals, formed in the reaction mother liquor, were separated, the diazoamino diazo salt was obtained sufficiently pure for analysis. This salt did not change the intensity of its coloring when stored in a moist state in air, as was the case with the 4-nitro analog, and it was stable to storage for 4–7 days, after which it also turned brown and deteriorated. It was also much more stable to light than the diazoamino diazo salt from 4-nitrodiazobenzene.

Analyses for the methylsulfamic acid radical content by nitrosation with nitrite in an acidic medium, as well as for the content of active and passive 3-nitrodiazobenzene radicals by combining first in a neutral and then in an acidic medium, gave values which agreed closely with theoretical calculations and proved conclusively that the structure of the diazoamino diazo salt (IV) corresponds to that of the material.



(IV)

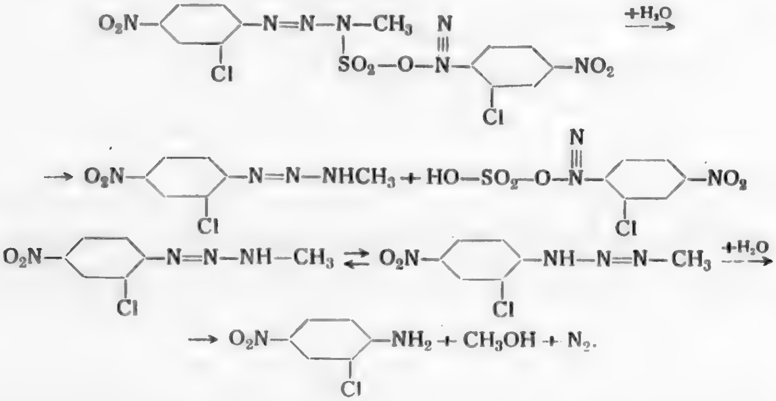
In this case, in contrast to the diazoamino diazo salt from 4-nitrodiazobenzene, the conversion of the passive diazo radical into the active form could be effected quantitatively. An elementary analysis for sulfur and nitrogen content further confirmed the formula proposed.

2-Nitrophenyldiazonium chloride and 4-nitro-2-chlorophenyl-

diazonium at a pH between 1 and 3 and temperatures from 0 to −6°, reacted with methylsulfamic acid, depositing at first, brownish yellow or brownish orange precipitates which immediately started to change into sticky brownish yellow tars which evolved nitrogen. By further treatment of these tars, it was possible to obtain amines, corresponding to the starting diazo compounds, for example, 4-nitro-2-chloroaniline, while sulfuric acid was detected in the mother liquors.

Attempts were made to obtain a diazoamino diazo salt from 2-nitrodiazobenzene and 4-nitro-2-chlorodiazobenzene by the second method, investigated for 4-nitrodiazobenzene and based on the exchange reaction between the potassium salt of the arylmethyltriazen-N-sulfonic acid and the chloride of the corresponding aryldiazonium. In this case, it turned out that in the first few seconds light yellow crystalline precipitates were formed much purer in appearance than those formed by the first method of synthesis, but in less than a minute they decomposed and were converted into the tars described above.

Thus, it was established that the 2-nitrophenyldiazonium salt of 2'-nitrophenyl-methyltriazen-N-sulfonic acid and the 4-nitro-2-chlorophenyldiazonium salt of 4'-nitro-2'-chlorphenylmethyltriazen-N-sulfonic acid are much less stable materials than the corresponding potassium salts, synthesized and investigated earlier [1, 4]. They are readily decomposed even in the first few minutes after formation giving finally the corresponding amines and sulfuric acid by the following reaction:



In contrast to the decomposition of the diazoamino diazo salt from 4-nitrodiazobenzene, in this case the reaction reached only the stage of 4-nitro-2-chloroaniline, which is incapable, under the given conditions, of entering into diazoamino condensation with 4-nitro-2-chlorodiazobenzene due to the fact that it is less base and, consequently, less active than 4-nitroaniline.

Thus, investigation of the reaction between methylsulfamic acid and four nitrodiazo compounds at pH from 1 to 3 showed that the latter were capable of undergoing diazoamino condensation with methylsulfamic acid in the cold in a practically acidic medium, i. e., under conditions where the combination of these diazo compounds with phenols or amines (β-naphthol, m-toluylendiamine, H acid) does not begin. Due to the low solubility in water of diazonium salts of arylmethyltriazen-N-sulfonic acids and the relatively slow rate of the diazoamino condensation reaction, diazoamino diazo salts are formed first. The latter, depending on the pH of the reaction medium are converted into other, more stable compounds, namely: at a higher pH— into potassium salts of arylmethyltriazen-N-sulfonic acids, while at low pH, in the case, for example, of 4-nitrodiazobenzene — into 4,4'-dinitrodiazoaminobenzene while in the case of the more "negative" 2-nitrodiazobenzene and 4-nitro-2-chlorodiazobenzene into the corresponding amines.

It seems likely that the formation of diazonium salts of methylsulfamic acid takes place even before the formation of diazonium salts of triazen-N-sulfonic acids. However, attempts to isolate the former using maximum concentrations of reagents in media of different degrees of acidity were unsuccessful, apparently, due to the high solubility of these salts.

EXPERIMENTAL

1. Reaction of methylsulfamic acid with 4-nitrodiazobenzene at pH 3. 6.9 g of 4-nitroaniline was dissolved in 24.0 ml of hydrochloric acid (containing 225 g/liter of HCl) by heating. On cooling externally with an ice-salt mixture, the solution crystallized; to the mass obtained was added 7.5 g of crushed ice and 10.5 ml of 5 N sodium nitrite (0.05 mole + 5% excess) in one addition. The diazonium solution formed was adjusted to pH 3 with a concentrated solution of sodium acetate, filtered and cooled to −2°.

Acetic acid was added to a solution of 7.9 g of potassium methylsulfamate in 30 ml of water until the pH was 3.

After cooling the solution to −2°, the cold solution of 4-nitrodiazobenzene was added to it. After several minutes stirring, a pale yellow precipitate began to form and the reaction mixture gradually turned into a paste. The precipitate was filtered off and well squeezed out on plates of unglazed porcelain so that the crystals became a bright, egg yellow. The filtrate gradually continued to deposit light yellow crystals, which, under the microscope, appeared as large, well formed blunt-ended needles or elongated prisms. As the crystals accumulated, they were filtered off, and added to the main precipitate. For recrystallization, the precipitate was dissolved in 50–60 times the amount of water, heated to 30–35° and the filtered solution was cooled to −2°. The light yellow, flocculent precipitate was filtered off, washed first with ice water and then with ether and afterwards pressed out and dried on a plate of unglazed procelain for 3–4 hours over solid sodium hydroxide and paraffin in a desiccator wrapped in black paper. The yield of the recrystallized diazo salt was 2.95 g. The next day the residual mother liquor gave a fresh yellow precipitate, but when a sample was filtered off,it only gave a weak reaction for active diazo compound (with a soda solution of H acid). This precipitate consisted of shiny, pale yellow crystals, which, after recrystallization, gave all the characteristic reactions of the potassium salt of (4'-nitrophenyl)-1-methyl-3-triazensulfonic acid-3 [1].

Under the microscope the recrystallized and dried diazo salt appeared to consist of fragments of elongated yellow prisms. On heating to 35–40° the diazo salt deflagrated with the formation of greenish yellow smoke. The freshly prepared aqueous solution of the diazo salt contained neither chlorine nor sulfate ions; its pH was about 5–6. After a day, the solution of diazo salt gave a reaction for mineral acid and a precipitate of $BaSO_4$ with barium chloride. Besides this, it deposited a precipitate showing all the characteristic properties of 4,4'-dinitrodiazoaminobenzene (solubility in an aqueous solution of sodium hydroxide with an intense violet – cherry color and the precipitation of bluish crystals with bronze iridescence on cooling; the formation of an intense cherry red color on heating with a solution of β-naphthylamine in glacial acetic acid). The dry diazo salt was very unstable. Even after 2–4 hours standing it began to turn brown and deteriorate. Deteriorating crystals placed on congo paper moistened with water gradually gave a blue spot, indicating that mineral acid was evolved. After a day's storage, the diazo salt was not completely soluble in water and its water extract contained sulfate ion. The dry diazo salt was sensitive to daylight, especially direct sunlight. After 5 minutes exposure to sunlight, the diazo salt changed from egg yellow to brown. Because of the extreme instability of the diazo salt, its analysis had to be carried out only on the freshly prepared product.

Found %: N 22.75., 22.92; S 7.49, 7.50; diazo nitrogen N 13.38, 13.33. $C_7H_8O_5N_4S$. (I) Calculated %: N 21.53; S 12.32; diazo nitrogen N 10.77. $C_{13}H_{13}O_8N_7S$. (II) Calculated %: N 22.94; S 7.50; diazo nitrogen N 13.11.

Thus, the elementary analysis confirmed that the diazo salt had the formula of the diazonium salt of arylmethyltriazen-N-sulfonic acid (II).

Analysis of the diazo salt by nitrosation. A sample of the salt was dissolved in 5 ml of concentrated hydrochloric acid in the cold over an hour, and the clear solution obtained was diluted with 50 ml of water and titrated with 0.05 N nitrite. The analysis data are given in Table 2.

Analysis by nitrosation also confirmed the formula $C_{13}H_{13}O_8N_7S$.

Analysis of the diazo salt for the active diazo group content. A sample of the diazo salt was dissolved in 100 ml of water at 25–27° and was acidified with one drop of glacial acetic acid. To the solution was added excess of a 0.05 N solution of m-toluylendiamine, it was mixed for 15–20 minutes and then the excess of azo components obtained was titrated with a 0.05 N solution of p-nitrophenyldiazonium. The data are given in Table 3.

The results of the analysis for the active diazo group content again confirmed the correctness of the formula $C_{13}H_{13}O_8N_7S$.

Analysis of the diazo salt for the total diazo group content by two methods. Method "a." A sample of the diazo salt was dissolved in 10 ml of concentrated hydrochloric acid and kept at room temperature for 2 hours. To the clear solution was added excess of a 0.05 N solution of the azo components, adjusted to the pH necessary for combination, it was mixed for 20 minutes and the excess of the azo components was titrated with a 0.05 N solution of p-nitrophenyldiazonium. If the combination was carried out with β-naphthol, the acid solution was neutralized to pH 7 with bicarbonate and if with m-toluylendiamine, then it was neutralized to pH 4 with sodium acetate.

TABLE 2

Sample Diazo Salt (g)	Amt. 0.05 N $NaNO_2$ solu. (ml)	Calc. amt. 0.05 N $NaNO_2$, based on Formula (ml)	
		(I)	(II)
0.2901	13.46	22.30	13.58
0.2398	11.32	18.43	11.22
0.3290	15.20	25.28	15.40

TABLE 3

Sample Diazo Salt (g)	Amt. 0.05 N m-toluylendiamine (ml)	Calc. amt. 0.05 N n-toluylendiamine, based on formula (ml)	
		(I)	(II)
0.2976	13.97	22.87	13.93
0.2996	13.75	23.03	14.02
0.2078	9.88	15.97	9.73

TABLE 4

Method of analysis	Sample of Diazo salt (g)	0.05 N solu. consumed (ml)		Calc. amt. 0.05 N azo compound, based on two diazo residues for Formula (II) (ml)	Actual amount consumed as % of calc.
		β-naphthol	m-toluylendiamine		
"a"	0.3481	26.80	—	32.8	81.7
	0.2878	—	21.30	26.44	79.1
"b"	0.2901	—	21.84	27.16	80.4
	0.2398	18.75	—	22.44	83.6
	0.3290	25.60	—	30.80	83.1

Method "b." A solution of a sample of the diazo salt in concentrated hydrochloric acid was first nitrosated quantitatively to destroy the methylsulfamic acid, then a solution of the azo component, adjusted to the required pH, was added and after 20 minutes the excess of the azo component was titrated with p-nitrophenyldiazonium. The results of the analyses by both methods are given in Table 4.

The actual consumption of the azo components in method "b" was slightly higher than in method "a" but did not amount to more than 83.6% of the amount which should be consumed by two diazo groups in the diazonium salt of arylmethyltriazen-N-sulphonic acid.

2. Synthesis of 4-nitrophenyldiazonium salt of (4'-nitrophenyl)-1-methyl-3-triazensulfonic acid-3, from potassium (4'-nitrophenyl)-1-methyl-3-triazensulfonate and 4-nitrophenyldiazonium. 1.49 g of potassium (4'-nitrophenyl)-1-methyl-3-triazensulfonate-3 was dissolved in 40 ml of water by moderate heating. On cooling to room temperature, part of the triazene precipitated as shiny crystals. A previously prepared solution of 4-nitrophenyldiazonium chloride was added with stirring to the suspension. A fine crystalline, egg yellow precipitate quickly formed and under the microscope a sample of it was found to consist of yellow needles, which did not differ in appearance from the crystals of the diazo salt prepared earlier from the reaction of 4-nitrophenyldiazonium with methylsulfamic acid (at pH 3). The diazo salt synthesized by the new method showed exactly the same properties as that prepared by the previous method after recrystallization from water, drying and storage. Final confirmation of the identity of the two diazo salts was given by analyses of the newly prepared product.

Found %: N 22.69; S 7.48. $C_{13}H_{13}O_8N_7S$. Calculated %: N 22.94; S 7.50.

3. Reaction of methylsulfaminic acid with 3-nitrodiazobenzene in a mineral acid medium. 3.28 g of potassium methylsulfamate was dissolved in 8–9 ml of water and externally cooled to $-2°$. With stirring, to this solution was added a previously prepared (by the method described for 4-nitrophenyldiazonium) hydrochloric acid solution of 0.02 N 3-nitrophenyldiazonium, cooled to $-4°$. After mixing the two solutions, the temperature was $-2°$ and the pH 1.5–1.6. After 5–6 minutes stirring, a flocculent, pale yellow precipitate with a brown tint, which formed, was filtered off and rejected as it was not a sufficiently homogeneous substance. On further stirring, and gradually raising the temperature to that of the room, there quite quickly formed a voluminous precipitate of a pure light yellow color, after which the solution turned into a paste. The precipitate was immediately filtered off and pressed out. During the following 3–4 hours, the mother liquor continued to deposit crystals, which were filtered and pressed out as they were formed, as when the diazo salt formed was allowed to stand for long in the mother liquor it became brown and rather impure. After standing overnight, the remaining filtrate deposited additional precipitate, but it was not completely homogeneous. All the intermediate fractions of crystals obtained were washed first with ice water, acidified with hydrochloric acid, and then with ether, pressed out well on an unglazed porcelain plate and dried in a desiccator overnight over solid alkali.

The diazo salt obtained was pale yellow crystals, which appeared as very elongated, flat, quadrangular plates under the microscope. The aqueous solution of the diazo salt was almost neutral (pH 6.5–6.8), did not contain sulfate or chloride ions and gave a reaction for an active diazo group with H acid. The solubility of the diazo salt in water was very low. Attempts to recrystallize it from water by the method described for the diazo salt from 4-nitrodiazobenzene and methylsulfamic acid, did not achieve the desired result as there was too little difference between the solubilities at the moderate temperatures, which had to be maintained to prevent decomposition of the product. It was also impossible to recrystallize the diazo salt without decomposition from alcohol, acetone and other solvents, acidified with mineral or organic acids. However, the intermediate fractions of the diazo salt, obtained as described above, were reasonably pure for the purpose of analysis.

In contrast to the 4-isomer, the diazo salt from 3-nitrodiazobenzene and methylsulfamic acid was relatively stable and it was possible to store it in a desiccator in the dark for 4–7 days without decomposition. On storing longer, it began to turn brown and change its properties and composition.

TABLE 5

Sample of Diazo Salt (g)	Amount of 0.05 N nitrite (ml)	Calculated amount of 0.05 N nitrite (ml)	
		(I)	(II)
0.1987	9.90	15.27	9.71
0.1131	5.51	8.69	5.53

The diazo salt was sensitive to light but to a relatively lower degree than the diazo salt from 4-nitrodiazobenzene.

Found %: N 23.35, 23.54; S 7.65, 7.8; diazo nitrogen N 13.52, 13.88. $C_7H_8O_5N_4S$. Calculated %: N 21.53; S 12.32; diazo nitrogen N 10.77. $C_{13}H_{13}O_8N_7S$. Calculated %: N 23.95; S 7.83; diazo nitrogen N 13.69.

Consequently, the elementary analysis confirmed the formula of the 3-nitrophenyldiazonium salt of (3'-nitrophenyl-methyltriazen-N-sulfonic acid) $C_{13}H_{13}O_8N_7S$.

TABLE 6

Sample of Diazo salt (g)	Actual amount of 0.05 N β-naphthol solution (in ml)	Calculated amount of 0.05 N β-naphthol solution (in ml)	
		(I)	(II)
0.2187	11.10	16.81	10.69
0.3093	15.95	23.77	15.11

Analysis of the diazo salt by nitrosation. A sample of the salt was dissolved in 20 ml of concentrated hydrochloric acid and 75 ml of water and titrated with 0.05 N nitrite solution at room temperature. The results obtained are given in Table 5.

Analysis of the diazo salt for the active diazo group content. A sample of the salt was ground up into a paste and dissolved in 150 ml of distilled water at 25°. The diazo salt solution was added to excess of a 0.05 N solution of β-naphthol, neutralized to pH 7 with acetic acid, stirred for 15–20 minutes and the excess β-naphthol titrated with a 0.05 N solution of p-nitrophenyldiazonium. The results obtained are given in Table 6.

Analysis of the diazo salt for the total diazo group content. A sample of the salt was dissolved in 120 ml of water, acidified with 1.0–1.5 ml of concentrated hydrochloric acid. To the solution was added excess of a 0.05 N solution of β-naphthol, slightly acidified with acetic acid, sodium bicarbonate was added until the pH was 7 and it was combined by stirring with the β-naphthol for 15–20 minutes. After this, the excess β-naphthol was titrated with 0.05 N p-nitrophenyldiazonium solution (Table 7).

TABLE 7

Sample of Diazo salt (g)	Actual amt. of 0.05 N β-naphthol (ml)	Calculated amt. of 0.05 N β-naphthol for (II) (ml)	Ratio of actual to calculated amount (in %)
0.3048	29.47	29.78	99.0
0.1135	10.78	11.09	97.2

Thus, analyses for the content of methylsulfamic acid residues, active diazo groups and total diazo groups confirm the formula $C_{13}H_{11}O_7N_7S$.

4. Reaction of methylsulfamic acid with 2-nitrodiazobenzene in an acid medium. A suspension of 1.38 g of 2-nitroaniline in 7.1 ml of hydrochloric acid (containing 154 g/liter of HCl) was externally cooled to 0° and while it was stirred, first 5–6 g of finely crushed ice and then in one addition, 2.1 ml of 5 N potassium nitrite solution was added. After 10 minutes, the almost clear solution was filtered to remove the slight suspension, the excess nitrous acid destroyed by the addition of a solution of sulfamic acid and it was cooled to −2°.

The solution of 2-nitrodiazobenzene was added to a solution of 1.56 g of potassium methylsulfamate in 7 ml of water, cooled to −4°.

As the solution remained transparent for 20–25 minutes, sodium bicarbonate was slowly added to it until the pH reached 3. This produced an orange-browm precipitate, which was immediately filtered off. It seemed very small and tarry. Later, the mother liquor deposited fresh precipitate, which at once turned to tar on the filter. Attempts to purify the precipitates collected were unsuccessful.

5. Reaction of potassium (2'-nitrophenyl)-1-methyl-3-triazensulfonate-3 with 2-nitrodiazobenzene. To a solution of 1.5 g of potassium (2'-nitrophenyl)-1-methyl-3-triazensulfonate-3 in 50 ml of water, cooled to 0°, was added an equivalent amount of a cold solution of 2-nitrophenyldiazonium chloride with stirring. A quite large, light yellow precipitate was quickly formed, but it at once began to decompose and deposit a brown, tarry substance on the walls of the vessel. Attempts to isolate the yellow precipitate quickly after its formation or at least to examine it under the microscope were unsuccessful due to the high rate of decomposition.

6. Reaction of methylsulfamic acid with 4-nitro-2-chlorodiazobenzene in an acid medium. 1.73 g of 4-nitro-2-chloroaniline and 5.5 ml of hydrochloric acid (containing 265 g/liter of HCl) were stirred on a boiling water bath until a homogeneous mass formed, then it was cooled externally to 0°, 4–5 g of finely crushed ice was added to lower the temperature to −6° and 2.1 ml of 5 N sodium nitrite solution was added. The suspension, which was converted into a solution after 8–10 minutes stirring, was filtered, the excess nitrous acid destroyed by the addition of sulfamic acid and it was cooled to −2°.

A solution of 1.56 g of potassium methylsulfamate in 4 ml of water, cooled to −6°, was added to the cold solution of 4-nitro-2-chlorophenyldiazonium chloride. The turbid solution immediately deposited a yellow-brown precipitate. At the same time the evolution of gas began. On the surface of the reaction mixture and on the walls of the vessel a reddish brown tar began to deposit. After several minutes of stirring, all the precipitate turned into a lump of a tarry material. The tar separated from the solution swelled up on standing, evolved gas and at the same time changed color from reddish brown to a dark tobacco color.

In order to free the tar from the mother liquor, which gave a reaction for active diazo groups, it was washed with water, when it became very yellow. Samples no longer combined with H-acid in the cold or on heating (both in acid and neutral media), which indicated that they no longer contained diazo groups. With aqueous and alcohol solutions of alkali hydroxides the tar did not give colors, which indicated the absence of nitrodiaryl-triazene.

On acidifying a sample of the tarry substance with hydrochloric acid, and adding nitrite, a diazo compound was formed, which combined with H acid to form a violet-red azo dye, which acquired a pure blue tint on adding alkali, i. e., it was 4-nitro-chlorodiazobenzene. Consequently, the tarry material contained 4-nitro-2-chloro-aniline.

7. Reaction of potassium (4'-nitro-2'-chloro)-1-methyl-3-triazensulfonate-3 with 4-nitro-2-chlorodiazo-benzene. To a concentrated aqueous solution of potassium (4'-nitro-2'-chloro)-1-methyl-3-triazensulfonate-3 was added an equivalent amount of 4-nitro-2-chlorophenyldiazonium at 0°. Immediately, a copious light yellow precipitate formed, immediately began to dissolve and disappeared after a few seconds. At the same time, a brown tarry deposit formed on the walls and the solution became turbid. Attempts to isolate the initially formed light yellow precipitate or at least to examine it under the microscope, were in vain as the diazo salt from 4-nitro-2-chlorodiazobenzene and methylsulfamic acid was unstable under the experimental conditions.

SUMMARY

1. The reaction of methylsulfamic acid with nitroaryldiazo compounds was investigated in acidic media and it was shown that under these conditions diazonium salts of aryl-1-methyl-3-triazensulfonic acids-3 were formed.

2. It was established that the synthesis of diazonium salts of aryl-1-methyl-3-triazensulfonic acids-3 may also be carried out by the exchange reaction between a diazonium chloride and potassium salts of aryl-1-methyl-3-triazensulfonic acids-3.

3. The properties and decomposition reactions of the diazonium salts of aryl-1-methyl-3-triazensulfonic acids-3 were studied. It was shown that their stability falls with an increase in the electrophilic nature of the substituents in the nucleus of the diazo radicals in their composition.

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HYDROPHILIC PROPERTIES AND HEATS OF SWELLING OF CHITIN

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Inspite of the widespread distribution of chitin in nature, its properties have been studied but little. In recent years, the work of S. N. Danilova and E. A. Plisko have contributed a great deal to the study of the properties of chitin and to the preparation of a series of its derivatives [1–3]. The results of this work indicate the real possibility of using chitin practically in the form of derivatives for the preparation of finishes, films and fibers.

The macromolecules of chitin are constructed similarly to cellulose and differ only in that, in each glucose ring, one of the hydroxyl groups of a secondary carbon atom is substituted by an acetylamino group. Inspite of the close similarity of the chemical structures of the cellulose and chitin macromolecules, they differ noticeably in reactivity. In contrast to cellulose, chitin does not swell much in alkali solutions, does not dissolve in a cuprammonium solution and forms ethers and esters much less readily.

On the basis of the investigations carried out, it seems likely that the large difference in reactivity of chitin and cellulose is due not only to the presence of the acetylamino group in chitin which replaces part of the reactivity of the hydroxyl groups, but also to the properties of their submicroscopic structure.

It was shown in the papers by S. N. Danilova and E. A. Plisko [1, 2] that by repeatedly freezing and defreezing, chitin in alkali solutions is not only swelled much more but could also be wholly dissolved in the alkali. The authors' explanation of this process was that the structure of chitin became friable, analogous to the phenomenon observed in cellulose fibers.

The study of cellulose fibers showed that their hydrophilic properties could give an idea of the state of the fiber structure, density of packing of the chain-like cellulose molecules and characterize the possible reactivity fiber in a number of cases [4]. It would be of considerable interest to study these properties for chitin so as to characterize its structure.

The purpose of this work was to study the hydrophilic properties and heats of swelling of chitin and to compare them with analogous data for cellulose fibers.

EXPERIMENTAL

For the investigation we used chitin from crab shells, purified as described earlier [1]. We carried out determinations of the hygroscopicity at relative humidities of 65 and 100%, the amount of unfrozen water in chitin after its saturation with water vapor, the heat of wetting with water and the heat of swelling in sodium hydroxide solutions. As the value of the specific heat capacity of the material investigated needed to be known for calculating the amounts of unfrozen water in it [5], it was determined calorimetrically for chitin as well. For this a sample of chitin was dried in vacuum over phosphorus pentoxide, cooled to a definite temperature and then placed in the calorimeter in a sealed tube. The specific heat capacity of chitin was derived from the heat effect of the calorimeter by the appropriate calculations. The measurements carried out showed that the specific heat capacity of chitin is somewhat higher than that of cellulose and is 0.373 ± 0.03 cal/g/degree.

The results of determining the hygroscopicity of chitin and the amount of unfrozen water in it after saturation with water vapor at 100% relative humidity are given in Table 1; for comparison we also give the values for cellulose fibers from ramie and mercerized viscose wood cellulose, whose hygroscopicity is very close to that of chitin.

It can be seen from the data in Table 1 that chitin has a hygroscopicity close to that of mercerized cellulose fibers and considerably greater than that of ramie fibers. However, the moisture absorbed by the chitin is almost wholly frozen at $-6°$, while ramie fibers still retain 12.5% of the water and the mercerized wood cellulose fibers — 26.2%.

TABLE 1

The Hydrophilic Properties of Chitin and Cellulose Fibers

Material investigation	Hygroscopicity (in % of wt. of dry material at relative humidity)		Amount of unfrozen water at $-6°$ after saturation at 100% rel. humidity (in % of wt. of dry material)
	65%	100%	
Chitin	8.9	34.7	1.4
Ramie fibers	5.5	19.7	12.5
Mercerized viscose wood cellulose fibers	8.96	32.6	26.2

As water molecules are most securely retained on an active inner surface of a hygroscopic material, the results given indicate that the chitin surface is less active and permeable to water in comparison with cellulose fibers. The moisture absorbed by chitin is probably in coarser capillaries, from which it is readily frozen when the temperature is lowered to $-6°$.

The values of the heat of swelling of chitin and cellulose fibers in water and alkali solutions are given in Table 2.

Chitin that is air dried and dried at 105° very readily becomes wet with water and the calorimetric measurements take several minutes. Air dried chitin also reacts very readily with solution of sodium hydroxide in concentrations of up to 23%. Cellulose fibers behave similarly; then readily become wet and swell and the equilibrium temperature is rapidly established in the calorimeter. The alkali reaction for both chitin and cellulose proceeds very slowly in higher concentrations of sodium hydroxide (34.5%). Thus, the equilibrium in the calorimeter is established $\frac{1}{2}$ an hour after immersion in the alkali solution for cellulose fibers and it takes 1 hour 10 minutes for chitin. Dried chitin does not become wet readily even in the lower concentrations of sodium hydroxide and due to this, the calorimetric data cannot be reliable. Taking the above into consideration, the heats of swelling were measured without drying the chitin, i. e., with some amount of absorbed moisture in it.

TABLE 2

Heats of Swelling of Chitin and Cellulose Fibers in Water and in Solutions of Sodium Hydroxide (20°)

Material investigated	Moisture in air-dried state (in %)	Heat of swelling (cal/g)						
		In water		In solutions of NaOH (for air-dried samples) at the concentrations of NaOH (in %)				
		sample dried at 105°	air dry sample	8	12	17.5	23	34.5
Chitin	8.90	12.4	3.3	—	3.8	6.7	8.6	76.9
Ramie fibers	5.50	11.9	3.7	8.8	21.5	28.1	—	63.3
Mercerized viscose wood cellulose fibers	8.96	17.3	4.5	13.9	22.5	26.8	—	54.7

The data in Table 2 show that the heat of wetting of chitin by water is almost the same as the value for ramie fibers and is less than that for mercerized cellulose. However, the air-dried cellulose fibers swell considerably in the reaction with sodium hydroxide and the heat effect of swelling in alkalis, even in low concentrations, is much greater than the value for the heat of wetting in water. Chitin, however, reacts very little with solutions of sodium hydroxide in concentrations of up to 17.5 %; the heat effect simply coresponds to the values of its wetting by water in the air-dried state. This effect increases slightly in 17.5 and 23% solutions of sodium hydroxide and increases sharply in a 34.5% solution, even exceeding the values for cellulose fibers. It is possible that this is due to splitting out of acetyl groups, which occurs in concentrated solutions of sodium hydroxide. Independent experiments were carried out with a chitin sample from which some of the acetyl groups had been removed by treatment with a 30% solution of sodium hydroxide at -30° (the sample contained 4.74% amino nitrogen and 6.46% acetyl groups as compared with the original chitin sample, which had 6.41% N and 20% acetyl groups). This chitin reacted somewhat more readily with sodium hydroxide solutions. Thus, for example, its heat of reaction with a 17.5% sodium hydroxide solution was 11.0 cal/g, while with a 34.5% solution it was 101;3 cal/g. The freezing of the chitin in alkali in preparing this sample probably made its structure more friable and more permeable to sodium hydroxide.

SUMMARY

1. The specific heat capacity of chitin is close in value to that of cellulose fibers and is 0.373 ± 0.03 cal/g/degree.

2. Moisture, absorbed at 100% relative humidity, by chitin, in contrast to cellulose fibers, freezes almost completely which indicates that chitin lacks a large active inner surface where the water molecules would be securely held.

3. A study of the heat of swelling of chitin in solutions of sodium hydroxide (concentrations up to 23%) indicated that the hydroxyl groups in chitin do not react readily with NaOH molecules. The data obtained show that the structure of chitin is less accessible to reagents than the structure of cellulose fibers, which is directly related to the low reactivity of chitin in esterification.

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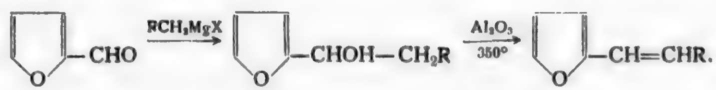
** Original Russian pagination. See C. B. Translation.

CATALYTIC HYDROGENOLYSIS IN FURAN COMPOUNDS

N. I. Shuikin and I. F. Belsky

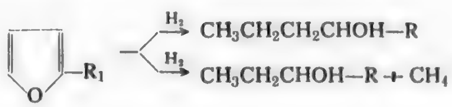
The investigation of the hydrogenolysis of furan and of its closest homologs that we had undertaken, showed that this reaction may be used for preparing certain difficultly accessible alcohols and ketones of the aliphatic series. As is known, α-alkenylfurans may be obtained from furfurol and lower alkyl halides, as a result of the following reactions:



A while ago, one of us [1–5] found the optimal conditions for the smooth catalytic hydrogenation of furan and a series of its homologs in the vapor phase under normal pressure with quantitative yields of the corresponding tetrahydrofurans. Further investigations [6, 7] showed that hydrogenolysis of the furan ring with the formation of alcohols and ketones of the aliphatic series occurred at temperatures higher than the optimal.

It was established (in agreement with Connor and Adkins [8]) that the furan ring undergoes hydrogenolysis much more readily than that of tetrahydrofurans. Using furan and its closest homologs as examples, we investigated the relative capacity of the C-O and C-C bonds of the ring for hydrogenolysis.

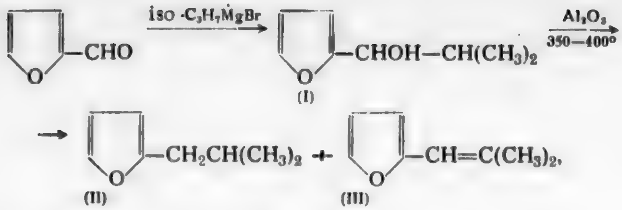
In this work we studied the reactions of α-isobutyl-, α-isobutenyl- and α-pentenylfuran during their hydrogenation on a Raney nickel catalyst at normal pressure. We thus found that, in agreement with our previous observations, the hydrogenation of these compounds at 175° resulted mainly in the formation of aliphatic alcohols and ketones— the products of hydrogenolysis of the furan ring:



where R_1 is isobutyl, isobutenyl or pentenyl, while R is isobutyl and n-amyl.

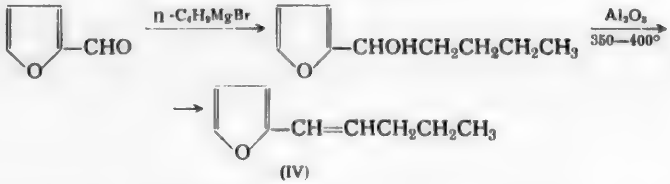
The hydrogenation of α-isobutyl-, α-isobutenyl- and α-pentenylfuran was carried out in a flowing system over a Raney nickel catalyst in excess hydrogen at 175°. The input rate of the material from an automatic buret was 0.06 $hr.^{-1}$. The catalyst was prepared by incomplete dissolving out of the aluminum with dilute sodium hydroxide from a Ni-Al alloy which contained 27% Ni, using the method described earlier by one of us [5].

α-Isobutenyl- (III) and α-isobutylfuran (II) were obtained as a result of the following reactions:



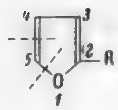
Paul [9] showed that together with alkenylfurans, alkylfurans were also formed in the dehydration of alkylfurylcarbinols.

α-Pentenylfuran (IV) was synthesized by the following scheme:



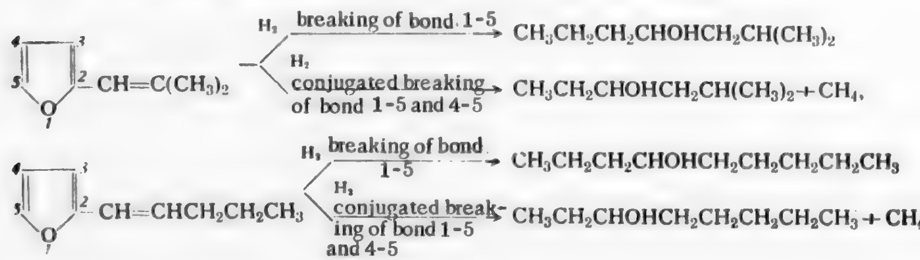
α-Isobutyl-, α-isobutenyl- and α-pentenylfurans in the presence of Raney nickel catalyst at 175° were converted, on the one hand, into the corresponding α-alkyltetrahydrofurans and on the other, underwent splitting of the furan ring with the formation of aliphatic alcohols and ketones. By hydrogenating α-isobutyl-, α-isobutenyl- and α-pentenylfurans under the conditions adopted, 26, 19 and 25% yields of α-alkyltetrahydrofurans were obtained, respectively. In this way the main part of the catalysates obtained consisted of products of the hydrogenolysis of the furan ring.

As shown by us earlier [6, 7], furan homologs that have either an alkyl or alkenyl substituent in the α-position, undergo hydrogenolysis of the ring mainly with breaking of the C-O bond 1—5 and conjugated breaking of the bonds 1—5 and 4—5.



The results of this investigation confirmed anew these rules governing the hydrogenolysis of the furan ring.

In agreement with the data in the previous paper, the hydrogenolysis of the compounds investigated proceeded mainly by the splitting of the furan ring at the C-O bond 1—5, as well as by the conjugated breaking of the bonds 1—5 and 4—5. Here, secondary alcohols and ketones corresponding to them were formed.



The primary alcohols, which could have formed as a result of the hydrogenolysis of the C-O bond 1—1, next to the substitutent, either were practically absent or were contained in the reaction products in very small amounts. The reason for this can be found in the screening effect of the side group on the adjacent C-O and C=C bonds.

The comparative hydrogenolysis of α-isobutyl- and α-isobutenylfuran carried out under identical conditions,

showed that the unsaturated side chain, in comparison with its saturated analog, increased somewhat the capacity of the furan ring for hydrogenolysis. The degree of splitting of the ring in α-isobutyl- and α-isobutenylfuran was 74 and 81% respectively.

EXPERIMENTAL

Isopropyl-α-furylcarbinol (I), was prepared (450 g) by a Grignard reaction between furfurol and isopropyl bromide in 73% yield and had the following properties:

B.p. 66–68° (3 mm), d_4^{20} 1.0297, n_D^{20} 1.4791, MR_D 38.6. $C_8H_{12}O_2$. calc. 39.2.

The dehydration of isopropyl-α-furylcarbinol was carried out over aluminum oxide at 350–400° with a volume rate of 0.3 hours^{-1}. The catalysate obtained was separated off from the water, dried with potash, heated to boiling with sodium in a flask with a reflux condenser for 3 hours and then fractionally distilled on a column with an efficiency of 30 theoretical plates. In agreement with Paul's data [9], we isolated α-isobutyl- and α-isobutenylfurans from the catalysate.

α-Isobutylfuran (II) had the following properties:

B.p. 128–128.5° (750 mm), d_4^{20} 0.8785, n_D^{20} 1.4415, MR_D 37.4. $C_8H_{12}O$. calc. 37.6.

α-Isobutenylfuran (III) had the following properties:

B.p. 155–156° (750 mm), d_4^{20} 0.9416, n_D^{20} 1.5140. MR_D 39.06. $C_8H_{10}O$. calc. 37.2.

The yields of α-isobutyl- and α-isobutenylfurans were 17 and 60% respectively, calculated on the starting isopropyl-α-furylcarbinol.

The conditions of synthesis of α-pentenylfuran, the methods of purification and isolation of the final product were the same as in the previous case.

n-Butyl-α-furylcarbinol (350 g) was prepared (68% yield) and had the following constants:

B.p. 113–114° (10 mm), d_4^{20} 1.0035, n_D^{20} 1.4784, MR_D 43.52. $C_9H_{14}O_2$. calc. 43.80.

α-Pentenylfuran, prepared in 67% yield, had the following constants:

B.p. 60–60.5° (7 mm), d_4^{20} 0.9176, n_D^{29} 1.5006. MR_D 43.7. $C_9H_{12}O$. calc. 41.8.

Hydrogenation of α-isobutyl- and α-isobutenylfuran. The experiments on the hydrogenation of α-isobutyl- and α-isobutenylfuran were carried out under the same conditions so as to elucidate the effect of the unsaturated bond on the capacity of the furan ring to undergo hydrogenolysis. In the reactions we used 170 g of α-isobutenylfuran and 50 g of α-isobutylfuran. The hydrogenation products obtained (165 g of catalysate from the α-isobutenylfuran and 48 g of catalysate from the α-isobutylfuran) were distilled then on a column with an efficiency of 30 theoretical plates. The individual substances isolated during the course of the distillation were identified by the determination of the physical constants and in some cases by preparing derivatives. The relative content of individual substances in intermediate fractions was determined from the value of the refractive index.

The hydrogenolysis products of α-isobutylfuran amounted to 74% and the ring of α-isobutenylfuran was split 81% under the same conditions. The remaining part of the catalysates consisted of α-isobutyltetrahydrofuran (26 and 19% respectively). The relative composition of the hydrogenolysis products of α-isobutyl- and α-isobutenylfuran was the same.

The following compounds were isolated from catalysate obtained by hydrogenation of α-isobutenylfuran (the yield is given in weight % of the catalysate):

1) 2-Methylhexanone-4 (14%):

B.p. 135–135.5 (758 mm) [10], d_4^{20} 0.8120, n_D^{20} 1.4070, MR_D 34.61. $C_7H_{14}O$. calc. 34.54.

Semicarbazone, m.p. 152°.

2) 2-Methylhexanol-4 (8%):

B.p. 147–148° (758 mm) [11], d_4^{20} 0.8331, n_D^{20} 1.4220, MR_D 35.44. $C_7H_{16}O$. calc. 36.05. *

3) α-Isobutyltetrahydrofuran (19%):

B.p. 149–150° (755 mm), d_4^{20} 0.8484, n_D^{20} 1.4265, MR_D 38.70. $C_8H_{16}O$. calc. 38.59.

4) 2-Methylheptanone-4 (25%):

B.p. 154.5–155° (752 mm) [12], d_4^{20} 0.8122, n_D^{20} 1.4100, MR_D 39.11. $C_8H_{16}O$. calc. 39.16.

Semicarbazone, m.p. 124°.

5) 2-Methylheptanol-4 (30%):

B.p. 164–164.5° (752 mm) [13], d_4^{20} 0.8162, n_D^{20} 1.4220, MR_D 40.54. $C_8H_{18}O$. calc. 40.67.

6) Fractions with b.p. 90–105° and 120–125° (4–5%), which on treatment with semicarbazide gave semicarbazones with m.p. 136.5° and 109–110°, indicating the presence of small amounts of pentanone-3 and hexanone-3 in these fractions.

Hydrogenation of α-pentenylfuran. The investigation of the products, obtained from the hydrogenation of 200 g of α-pentenylfuran, was carried out in the same way as in the previous experiment. The following compounds were isolated and identified from the catalysate (192 g) (the yield is given in weight % of the catalysate):

1) Octanone-3 (11%):

B.p. 168–168.5° (750 mm) [14], d_4^{20} 0.8264, n_D^{20} 1.4178, MR_D 39.06. $C_8H_{16}O$. calc. 39.16.

Semicarbazone m.p. 92–93°.

2) Octanol-3 (3.3%):

B.p. 175–176° (745 mm) [15], d_4^{20} 0.8344, n_D^{20} 1.4270, MR_D 40.10. $C_8H_{18}O$. calc. 40.60.

3) α-Amyltetrahydrofuran (25%):

B.p. 181–182° (750 mm) [16], d_4^{20} 0.8532, n_D^{20} 1.4323, MR_D 43.26. $C_9H_{18}O$. calc. 43.21.

4) Nonanone-4 (36.3%):

B.p. 186–187° (745 mm) [17], d_4^{20} 0.8257, n_D^{20} 1.4204, MR_D 43.70. $C_9H_{18}O$. calc. 43.77.

Semicarbazone m.p. 85°.

5) Nonanol-4 (19.2%):

B.p. 191–192.5° (750 mm) [18], d_4^{20} 0.8263, n_D^{20} 1.4292, MR_D 45.03. $C_9H_{20}O$. calc. 45.29.

6) Nonanol-1 (3.3%):

B.p. 213–214° (750 mm) [19], d_4^{20} 0.8290, n_D^{20} 1.4330, MR_D 45.22. $C_9H_{20}O$. calc. 45.29.

* The somewhat low value of the molecular refraction of 2-methylhexanol-4 is apparently explained by small traces of α-isobutyltetrahydrofuran.

7) From a fraction with b.p. 121–125° (2%), we isolated a semicarbazone with m.p. 109.5°. This semicarbazone indicated the presence of hexanone-3 in this fraction.

SUMMARY

1. The hydrogenation and hydrogenolysis of α-isobutyl-, α-isobutenyl- and α-pentenylfurans was investigated on a Raney nickel catalyst at 175° in a flowing type of system. It was shown that under these conditions the ring of the above compounds underwent splitting by 74, 81 and 75% respectively.

2. It was established that the main direction of the hydrogenolysis of α-isobutyl-, α-isobutenyl- and α-pentenylfurans was breaking of the C-O bond 1–5 and conjugated breaking of the 1–5 and 4–5 bonds, and as a result, secondary aliphatic alcohols and ketones corresponding to them were formed.

3. The hydrogenolysis of furan homologs could be proposed as a method of preparing certain difficultly accessible alcohols and ketones of the aliphatic series.

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* T. p. = C. B. Translation pagination.

** Original Russian pagination. See C. B. Translation.

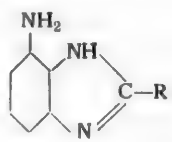
INVESTIGATION IN THE FIELD OF IMIDAZOLE DERIVATIVES

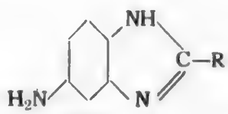
XVI. THE BASICITY OF ISOMERIC 4- AND 6-AMINO-3-METHYLBENZIMIDAZOLES*

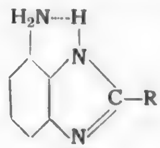
L. S. Efros and B. I. Ionin

In one of the preceding reports [1], in comparing the basicity constants of isomeric 4- and 6-aminobenzimidazoles, we showed that amino groups situated in positions 4 (I) and 6 (II) of the benzimidazole molecule have different effects on the basicity of the compound. At the same time that the amino group in position 6 increases the basicity constant of benzimidazole by approximately 20 times, the amino group in position 4 hardly affects it at all. This phenomenon was explained by the absence of conjugation between the amino group in position 4 and the hetero ring. However, another explanation seemed possible.

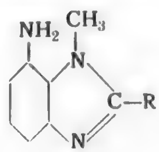
The steric proximity of the amino group in position 4 and the NH group of the hetero ring in one of the tautomeric forms (I) formed a basis for a hypothesis on the existence of a hydrogen bond (III). The latter may be the reason for the lack of effect that this amino group has on the basicity of the compound.


(I)


(II)


(III)

We decided to check this hypothesis in the present work, by determining the basicity constants of isomeric 4- and 6-amino-3-methylbenzimidazoles (IV) and (V), in which a hydrogen bond is impossible.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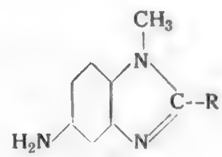
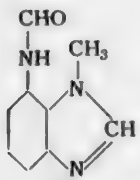

(V)

The starting material for the synthesis of a compound of general structure (IV) was 2,6-dinitrochlorobenzene [2], from which, 2,6-dinitromethylaniline was obtained by treatment with an aqueous solution of methylamine. This product was reduced with tin and hydrochloric acid to 2,6-diaminomethylaniline, which was isolated in the form of the readily oxidized hydrochloride by precipitation with concentrated hydrochloric acid from an aqueous solution. Due to its instability, this compound could not be isolated in an analytically pure state and characterized. However, on boiling for a long time with anhydrous formic acid and with glacial acetic acid it gave 4-formylamino-3-methylbenzimidazole (VI) and 4-acetylamino-2,3-dimethylbenzimidazole (VII), respec-

*For report XV see J. Gen. Chem., 27, 127 (1957).

tively, which crystallized well from water in the form of colorless needles.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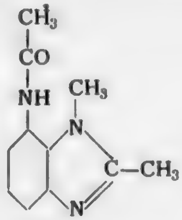
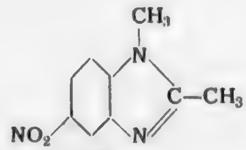

(VII)


(VIII)

By boiling the latter with hydrochloric acid, dihydrochlorides of 4-amino-3-methylbenzimidazole (IV, where R=H) and 4-amino-2,3-dimethylbenzimidazole (IV, where $R=CH_3$) were obtained.

2-Amino-4-nitromethylaniline was used as the starting material for the synthesis of 6-amino-2,3-dimethylbenzimidazole (V, where $R=CH_3$). Condensation of the former with acetic acid in a hydrochloric acid medium gave 6-nitro-2,3-dimethylbenzimidazole (VIII), whose nitro group was then reduced with tin and hydrochloric acid. 2,3-Dimethylbenzimidazole, required for comparison, was obtained by the usual method from o-nitromethylaniline.

The compounds synthesized were titrated potentiometrically with a glass electrode on a valve potentiometer LP-5. The hydrolysis pK values found are give in Table 1.

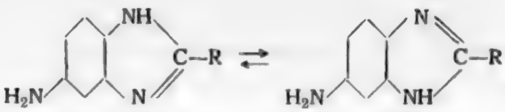
TABLE 1

Hydrolysis pK of Benzimidazole Derivatives

No. of sample	Product examined	Hydrolysis pK	
		pK_1	pK_2
1	3-Methylbenzimidazole	5.57 [3]	—
2	4-Amino-3-methylbenzimidazole	5.79	2.36
3	6-Amino-3-methylbenzimidazole	6.21	3.29
4	2,3-Dimethylbenzimidazole	6.55	—
5	4-Amino-2,3-dimethylbenzimidazole	6.66	2.35
6	6-Amino-2,3-dimethylbenzimidazole	7.00	3.38

It can be seen from the data in the table that the amino group in position 4 of 3-methyl derivatives of benzimidazole, as in the case of the compounds not containing a methyl group in position 3 studied previously, has a very weak effect on the basicity of the benzimidazole derivatives, while at the same time, the amino group in position 6 increases the basicity by 4 to 6 times. This again confirms the accuracy of the explanation given for this phenomenon earlier [1] and makes it possible to refute the hypothesis that the formation of a hydrogen bond explained why the amino group situated in position 4 had no effect on the basicity of the compound.

However, the amino group in position 6 has a much smaller effect in the compounds investigated than in the case of benzimidazole derivatives which do not contain a methyl group in position 3, and whose basicity constant increases on an average of 20 times under the effect of the amino group. This indicates, apparently, that the main tautomeric form of the latter compounds, which are capable of tautomerism, is not (II), to which the methylated products (V) correspond, but (IX):



(II) (IX)]

A study of the second hydrolysis constants of isomeric 4- and 6-amino-3-methylbenzimidazoles shows that, the same as in the case of derivatives not containing a methyl group in position 3, the basicity of the amino group in position 4 is much smaller than the basicity of the amino group in position 6.

EXPERIMENTAL

2,6-Diamino-N-methylaniline. Into a round-bottomed flask was placed 24 g of granulated tin and 60 ml of concentrated hydrochloric acid. The mixture was heated until reaction began and then 6 g of 2,6-dinitro-N-methylaniline (m.p. 104° [4]) was introduced in small portions. When all the dinitro compound had dissolved, the contents of the flask were diluted to 300 ml with water, filtered and the tin was precipitated electrolytically. The aqueous solution of the dihydrochloride of 2,6-diamino-N-methylaniline was evaporated to dryness in vacuum. The yield was about 2 g.

The product was purified by precipitation from a concentrated aqueous solution with strong hydrochloric acid. The pure product consisted of colorless crystals, which quickly darkened on standing in air in the moist state.

3-Methyl-4-aminobenzimidazole. Into a flask with a reflux condenser was placed 2 g of 2,6-diamino-N-methylaniline and 15 ml of formic acid, distilled over boric anhydride. The mixture was boiled for 3 hours, after which it was evaporated almost to dryness in a porcelain dish. The residue was dissolved in 50 ml of warm water and neutralized with ammonia. The precipitate thus formed was filtered off. After recrystallization from water, we obtained about 2.5 g of colorless needles of 3-methyl-4-formyl-aminobenzimidazole with m.p. 150°.

Found %: C 61.41, 61.72; H 4.97, 5.01; N 24.30. $C_9H_9ON_3$. Calculated %: C 61.72; H 5.14; N 24.00.

1.65 g of 3-methyl-4-formylaminobenzimidazole was dissolved in 10 ml of 10% hydrochloric acid and refluxed for 1 hour, after which the solution was treated with active charcoal and filtered. On cooling, colorless crystals of the dihydrochloride of 3-methyl-4-aminobenzimidazole precipitated. The yield was about 1.5 g., the product melted at 284–285°.

Found %: C 43.82, 43.65; H 4.82, 5.35; N 19.16, 19.30. $C_8H_{11}N_3Cl_2$. Calculated %: C 43.64; H 5.03; N 19.10.

In a potentiometric titration (Fig. 1), 0.1925 g of substance consumed 9 ml of alkali (0.0952 M NaOH). Found M 225. Calculated M 220.0.

0.5 g of the dihydrochloride of 3-methyl-4-aminobenzimidazole was dissolved in the minimum quantity of water and 40% sodium hydroxide was added until the precipitate thus formed did not noticeably increase in volume. The precipitate was filtered off and recrystallized from chlorobenzene. The yield was about 0.2 g. The slightly reddish crystals of the base 3-methyl-4-aminobenzimidazole melted at 167–168°.

2,3-Dimethyl-4-aminobenzimidazole. 2,3-Dimethyl-4-acetylaminobenzimidazole was prepared similarly to the formyl deriviative of 3-methyl-4-aminobenzimidazole by boiling 2 g 2,6-diamino-N-methylaniline with 30 ml of acetaldehyde for 8 hours. The yield was about 2 g of colorless needles with m.p. 199.5°.

Found %: C 64.82; H 6.54; N 20.80. $C_{11}H_{13}ON_3$. Calculated %: C 65.03; H 6.40; N 20.68.

Colorless crystals of the dihydrochloride of 2,3-dimethyl-4-aminobenzimidazole were prepared and purified similarly to the corresponding derivative of 3-methyl-4-aminobenzimidazole from 3 g of 2,3-dimethyl-4-acetylaminobenzimidazole and 10 ml of 10% hydrochloric acid with a yield of about 2.5 g. The product melted at 302°.

Found %: C 46.05, 45.98; H 5.30. 5.21; N 17.93, 17.78. $C_9H_{13}N_3Cl_2$. Calculated %: C 46.15; H 5.55; N 17.95.

In a potentiometric titration (Fig. 2), 0.2164 g of substance consumed 9.5 ml of alkali (0.0952 M NaOH). Found M 239. Calculated M 234.0.

0.5 g of the dihydrochloride of 2,3-methyl-4-aminobenzimidazole was dissolved in the minimum amount of water and a little 35% NaOH solution was added. The precipitate thus formed was filtered off and washed on the filter with a small amount of cold water. Then the precipitate was dissolved in warm acetone and the solution was treated with activated charcoal, filtered and gradually diluted with 4–5 times its volume of ether. On cooling, there precipitated about 0.2 g of colorless crystals of the base 2,3-dimethyl-4-aminobenzimidazole, which melted at 150–151°.

2,3-Dimethylbenzimidazole [5]. In a potentiometric titration on 0.0422 g of 1,2-dimethylbenzimidazole with m.p. 115.5°, dissolved in 12 ml of 0.1 N hydrochloric acid, 3.0 ml of alkali (0.0952 M NaOH) was consumed. Found M 148. Calculated M 146.

The potential at the half equivalence point corresponded to pH 6.55.

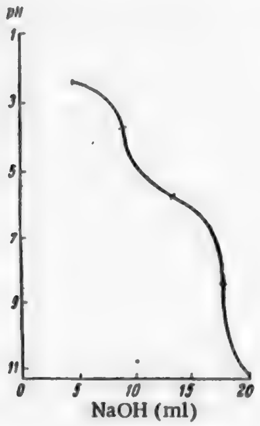


Fig. 1. Potentiometric titration of 3-methyl-4-aminobenzimidazole.

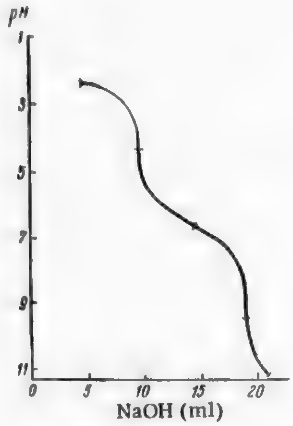


Fig. 2. Potentiometric titration of 2,3-dimethyl-4-aminobenzimidazole.

2,3-Dimethyl-6-aminobenzimidazole. Into a wide tube was placed 2.5 g of granulated tin and 10 ml of concentrated hydrochloric acid. The mixture was heated until reaction began and then 1 g of 2,3-dimethyl-6-nitrobenzimidazole [6, 7] was gradually introduced in the form of the hydrochloride (m.p. 272° with decomp.). When all the nitro compound had dissolved, the hot solution was separated from the unreacted tin and the tin complex, which precipitated on cooling, was dissolved in water and the tin precipitated electrolytically. The solution was boiled with active charcoal, filtered and evaporated to dryness. The dry residue was dissolved in a small amount of aqueous alcohol and slightly reddish crystals of the dihydrochloride of 2,3-dimethyl-6-aminobenzimidazole were precipitated by adding ether. The yield was about 0.3 g and the m.p. 301°.

Fig. 3. Potentiometric titration of 2,3-dimethyl-6-aminobenzimidazole.

Found %: C 45.88, 46.05; H 5.99, 6.40; N 18.07. $C_9H_{13}N_3Cl_2$. Calculated %: C 46.15; H 5.55; N 17.95.

In a potentiometric titration (Fig. 3), 0.0527 g of substance consumed 2.35 ml of alkali (0.0952 M NaOH). Found M 235.5. Calculated M 234.

SUMMARY

1. A comparison of the basicity constants of the derivatives of 4-amino-3-methylbenzimidazole with the constants of analogous derivatives of 6-amino-3-methylbenzimidazole shows that in this series the amino group in position 4, in contrast to the amino group in position 6, has almost no effect on the basicity of the compounds.

2. The breakdown of conjugation between the amino group in position 4 and the nitrogen atom of the hetero ring of benzimidazole explains why this amino group has no effect on basicity.

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* T. p. = C. B. Translation pagination.

** In Russian.

THE SYNTHESIS OF BENZIMIDAZOLE COMPOUNDS CONTAINING THE BIS –(β–CHLOROETHYL) – AMINO GROUP

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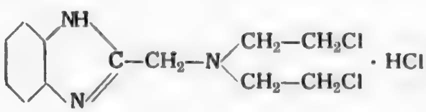
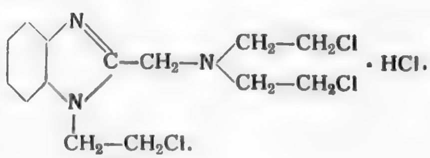
and S. M. Lotareichik

As is known, the physiological activity of compounds containing the bis-(β-chloroethyl)-amino group, depends to a large extent, on the character of the radicals bonded to it. Considering that there are compounds among the benzimidazole derivatives which are interesting from the point of view of their physiological action, together with L. F. Larionov, we decided that it would be advantageous to study the physiological activity of such materials in which the bis-(β-chloroethyl)-amino group was bonded to the benzimidazole grouping. For this, we carried out the synthesis of the hydrochlorides of 2-bis-(β-chloroethyl)-aminomethylbenzimidazole (I) and 1-β-chloroethyl-2-bis(β-chloroethy)-aminomethylbenzimidazole (II):

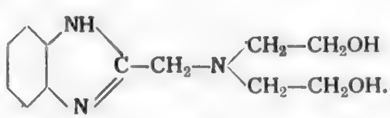


(I)



(II)

Compound (I) was obtained from 2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole (III) which in its turn had been synthesized from 2-chloromethylbenzimidazole and diethanolamine.



(III)

The condensation of 2-chloromethylbenzimidazole with diethanolamine was carried out in an acetone medium in the presence of sodium acetate or by heating 2-chloromethylbenzimidazole in excess diethanolamine. Compound (III) was isolated in the form of a picrate from the viscous mass formed as a result of the reaction. Decomposition of the compound with concentrated hydrochloric acid gave the hydrochloride of compound (III) from which compound (I) was obtained by the action of thionyl chloride in a chloroform medium. The synthesis of compound (II) was carried out in an analogous way, starting with 1-β-hydroxyethyl-2-chloromethylbenzimidazole.

EXPERIMENTAL

1. The picrate of 2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole. a) 4.2 g of unpurified 2-chloromethylbenzimidazole (m.p. 139–140°) and 6.0 g of diethanolamine were continuously stirred and heated on a boiling water bath for 4.5 hours. The black tarry mass obtained was dissolved in 150 ml of hot water. The aqueous

solution was filtered and the calculated amount of a 4% aqueous solution of picric acid was added to the filtrate with stirring. After 2 hours, the precipitated picrate was filtered off, washed on the filter with cold water and dried. The yield was 11.0 g (63.2%).

b) 11.0 g of 2-chloromethylbenzimidazole was mixed with 5.4 g of anhydrous sodium acetate, 7.0 g of diethanolamine and 130 ml of acetone. The mixture obtained was heated under reflux on a water bath for 4.5 hours. After heating, the acetone solution was filtered and the acetone distilled off from the filtrate. After distilling off the acetone, a viscous, dark brown mass remained, from which we obtained the picrate of 2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole by the method described above. The yield was 29.9 g (65.3%).

After recrystallization from water, we obtained a picrate with m.p. 186°. It was readily soluble in acetone and alcohol.

Found %: N 18.65, 18.63; $C_6H_2(OH)(NO_2)_3$ 65.92. M 694.0. $C_{12}H_{17}O_2N_3 \cdot 2C_6H_3O_7N_3$. Calculated %: N 18.18; $C_6H_2(OH)(NO_2)_3$ 66.08. M 693.2.

The hydrochloride of 2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole. 35 g of finely powdered picrate of 2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole was carefully ground in a mortar with 140 ml of concentrated hydrochloric acid. 210 ml of benzene was added to the suspension obtained and after shaking in a separating funnel, the benzene solution of picric acid was separated off from the solution of the hydrochloride of 2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole. The latter was washed 6–7 times with small amounts of benzene until the picric acid was completely removed.

The solution of the hydrochloride of 2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole was diluted with an equal volume of water, boiled with active charcoal, filtered and evaporated to dryness on a water bath. The residue was dissolved in 50 ml of ethyl alcohol, the solution was evaporated down. The operation of dissolving in alcohol and evaporating down was carried out 3 times, after which the mass solidified into a grey melt, which was ground in a mortar with 25 ml of anhydrous ethyl alcohol. 25 ml of anhydrous acetone was added to the suspension obtained. After an hour the precipitate was filtered off and washed on the filter with small amounts of a mixture, composed of equal amounts of anhydrous alcohol and acetone. The yield was 12.5 g (81.1%).

The hydrochloride of 2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole was a white powdery substance with m.p. 184–186°, soluble in water, carbon tetrachloride and benzene and insoluble in chloroform and anhydrous acetone.

Found %: N 13.85; HCl 23.60. M 312. $C_{12}H_{17}O_2N_3 \cdot 2HCl$. Calculated %: N 13.65; HCl 23.70. M 308.1.

The hydrochloride of 2-bis-(β-chloroethyl)-aminomethylbenzimidazole. 25 ml of thionyl chloride, mixed with an equal volume of chloroform, was slowly added, dropwise, to a suspension of 11.0 g of the hydrochloride of 2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole in 110 ml of chloroform. The mixture was refluxed on a water bath for 3.5 hours and left at room temperature for 3 days. Then the chloroform and thionyl chloride were distilled off in vacuum. In doing this the reaction mixture was either not heated at all or heated on a water bath no higher than 30–35°. The dry residue was mixed with 25 ml of chloroform, which was then completely distilled off in vacuum. This was done 3 times. The product obtained was treated consecutively with several portions (200 ml each) of anhydrous acetone, stirring and refluxing until the chloro derivative completely dissolved. The acetone solutions were combined, treated with active charcoal, filtered and concentrated to $^1/_4$ of the initial volume. On slow cooling, the hydrochloride of 2-bis-(β-chloroethyl)-aminomethylbenzimidazole crystallized out from the solution. This product could be isolated from the acetone solution, when it had been evaporated down to half the initial volume, by slowly adding to it an equal (by volume) amount of absolute ether. After 1 hour, the precipitated product was filtered off and dried. The yield was 10.0 g (91%).

The hydrochloride of 2-bis-(β-chloroethyl)-aminomethylbenzimidazole was a white crystalline substance with m.p. 154–155°, soluble in water, alcohol and hot acetone and insoluble in ether, benzene and carbon tetrachloride.

Found %: N 13.85; 13.50; HCl 11.95, 11.70; Cl 34.80, 34.80. M 311. $C_{12}H_{15}N_3Cl_2 \cdot HCl$. Calculated %: N 13.65; HCl 11.80; Cl 34.55. M 308.5.

1-β-Hydroxyethyl-2-chloromethylbenzimidazole. A mixture of 3.5 g of N-(β-hydroxyethyl)-o-phenylenediamine and 3.3 g of chloroacetic acid were dissolved in 21 ml of 15% hydrochloric acid and refluxed for 3 hours. The next day, the dark, but completely clear, reaction liquid was neutralized with sodium bicarbonate with external cooling in ice: at first dry – until the appearance of a precipitate, and then a 9% aqueous solution until it gave an alkaline reaction. The precipitate was filtered off, washed with cold water, carefully pressed out on the filter and dried in air.

For purification, the product obtained was dissolved in dilute hydrochloric acid, the solution shaken at room temperature with active charcoal till colorless, filtered and neutralized with a 9% solution of sodium bicarbonate. The precipitate was filtered off. The yield of pure product was 3.78 g (78.1%).

The 1-β-hydroxyethyl-2-chloromethylbenzimidazole obtained was a white powdery substance with m.p. 136–137°. It was readily soluble in acetone and ethyl acetate, difficultly soluble in benzene and insoluble in ether.

Found %: N 13.27; Cl 17.0. $C_{10}H_{11}ON_2Cl$. Calculated %: N 13.30; Cl 16.86.

The picrate of 1-β-hydroxyethyl-2-bis-(β-hydroxyethyl)-amino-methylbenzimidazole. 10.5 g of diethanolamine and 200 ml of acetone was added to a mixture of 21.0 g of 1-β-hydroxyethyl-2-chloromethylbenzimidazole and 8.2 g of anhydrous sodium acetate. The reaction mixture obtained was refluxed on a water bath for 3.5 hours. After cooling, the precipitate was filtered off and washed with a small amount of acetone. The acetone was distilled off from the filtrate and the syrupy mass formed dissolved in 100 ml of water. The solution obtained was poured into a hot solution of 45.8 g of picric acid in 1700 ml of water. A voluminous yellow precipitate was thus formed. The suspension was brought to the boil and then left at room temperature until the following day. The picrate obtained was filtered off. After crystallization from water it had m.p. 178–179°. The yield was 39.2 g (53.5%).

Found %: N 16.90, 16.89. $C_{14}H_{21}O_3N_3 \cdot 2C_6H_3O_7N_3$. Calculated %: N 17.11.

The hydrochloride of 1-β-hydroxyethyl-2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole. 39.2 g of carefully powdered picrate of 1-β-hydroxyethyl-2-(β-hydroxyethyl)-aminomethylbenzimidazole was mixed with 160 ml of concentrated hydrochloric acid. 300 ml of benzene was added to the suspension obtained and after shaking vigorously, the benzene solution of picric acid was separated off from the hydrochloric acid solution. The latter was washed 7 times with small amounts of benzene. The dark hydrochloric acid solution was diluted with water and boiled with active charcoal, after which it was filtered and concentrated on a water bath. The residue was dissolved in 40 ml of ethyl alcohol and the solution obtained was again evaporated down. The operation of dissolving in alcohol and evaporating down was carried out 3 times. The residual syrupy mass was left until the next day, when it partially crystallized. Dry acetone was added. The initially viscous product gradually solidified with mixing and triturating and was converted into a white powder, which was filtered off, washed several times with anhydrous acetone and dried at 50–60°. The yield was 16.3 g. The product obtained did not have a sharp melting point.

The hydrochloride of 1-β-chloroethyl-2-bis-(β-chloroethyl)-aminomethylbenzimidazole. 3.2 g of carefully powdered 1-β-hydroxyethyl-2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole hydrochloride was placed in a round bottomed reaction vessel with a tube, connected to a calcium chloride tube. With continuous cooling of the reaction vessel in ice, 10.5 ml of thionyl chloride was added dropwise at such a rate that the reaction did not proceed too vigorously. At the end of the thionyl chloride addition, which took about 2 hours, the reaction mixture was a homogeneous, yellow liquid. The reaction mixture was left a further 2 hours on an ice bath and then for 12 hours at room temperature, after which, the volatile products were distilled off in vacuum. The residual reddish yellow mass was dissolved in chloroform, heated with active charcoal and filtered. On adding absolute ether and cooling, the colorless solution yielded the reaction product, which was filtered off and dried at room temperature. The compound obtained was a white crystalline substance with m.p. 132–134°. The yield was 2.92 g (86.6%).

Found %: N 11.67; Cl 38.34, 38.45; HCl 9.57, 9.58. $C_{14}H_{18}N_3Cl_3 \cdot HCl$. Calculated %: N 11.33; Cl 38.27; HCl 9.84.

SUMMARY

2-Bis-(β-chloroethyl)-aminomethylbenzimidazole and 1-β-chloroethyl-2-bis-(β-chloroethyl) aminomethylbenzimidazole were formed from 2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole and 1-β-hydroxyethyl-2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole by the action of thionyl chloride on these compounds. In their turn, 2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole and 1-β-hydroxyethyl-2-bis-(β-hydroxyethyl)-aminomethylbenzimidazole may be obtained as a result of the condensation of diethanolamine with 2-chloromethylbenzimidazole and 1-β-hydroxyethyl-2-chloromethylbenzimidazole.

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HALOARYLATION OF UNSATURATED COMPOUNDS WITH AROMATIC DIAZO COMPOUNDS

III. THE REACTION OF 4-CHLORO-1-PHENYLBUTENE-2 WITH POTASSIUM HYDROXIDE AND A NEW METHOD OF SYNTHESIZING α-PHENYLBUTADIENE

A. V. Dombrovsky and A. P. Terentyev

The method of chlorophenylating butadiene-1,3, developed by us [1] makes it possible to obtain simply, and in good yields (70%) 4-chloro-1-phenylbutene-2 (I), synthesized from divinyl and diazotized aniline in an aqueous-acetone solution in the presence of cupric chloride and lime. An extremely reactive allyl chlorine and a labile hydrogen atom in position 1 are found in the molecule (I).

Of the numerous reactions into which (I) can enter, it seemed interesting to study the splitting off of the hydrogen chloride to obtain α-phenylbutadiene (II) which is usually synthesized by rather complicated methods. (II) is most often obtained from cinnamaldehyde by treatment with methylmagnesium iodide with subsequent dehydration of the carbinol formed [2–4]. Isagulyants and Esyan [5] described the preparation of (II) in 21–22 % yield by boiling 3-chloro-1-phenylbutene-2 with a 12-fold amount of powdered potassium hydroxide in toluene.

α-Phenylbutadiene is of interest, as it condenses spontaneously and under appropriate conditions may be converted into high molecular compounds. The polymerization of (II) and the structure of its polymers were investigated by Lebedev and Ivanov [6]. One of us studied the kinetics of the polymerization of (II) [3] using the method of diazometric determination of diene hydrocarbons developed by us.

In this article we describe experiments on the study of the effect of potassium hydroxide under various conditions which resulted in good yields of (II).

It is known that 1-p-nitrophenylbutene-2 is readily converted in a methanol solution of potassium hydroxide into α-p-nitrophenylbutadiene [7]. It was shown in paper [1] that (I) reacted with alcohol solutions of sodium alcoholate in two ways: (II) and 1-phenyl-4-alkoxybutene-2 were formed in almost equal amounts. In connection with this, we studied the effect on (I) of potassium hydroxide in methyl, ethyl, n-propyl and n-butyl alcohols. The experiments showed that the reaction of (I) with potassium hydroxide in these alcohols also proceeded in two directions: a) exchange of the chlorine atom for an alkoxyl group and, as a result, the formation of ethers, 1-phenyl-4-alkoxybutenes-2 and b) the splitting out of HCl and the formation of (II):

$$\underset{(I)}{C_6H_5CH_2CH{=}CHCH_2Cl} \longrightarrow \begin{cases} C_6H_5CH_2CH{=}CHCH_2OAlk \\ \underset{(II)}{C_6H_5CH{=}CHCH{=}CH_2} \end{cases}$$

The process of ether formation dominated.

TABLE

1-Phenyl-4-alkoxybutene-2

Formula	Yields, in %		Boiling point	n_D^{20}	d_4^{20}	MR_D	
	ethers	(II)				found	calculated
$C_6H_5CH_2CH{=}CHCH_2OCH_3$.	66.7	26.1	109°(11 mm)	1.5180	0.9573	51.35	50.73
$C_6H_5CH_2CH{=}CHCH_2OC_2H_5$.	60	25	102 (3mm)	1.5115	0.9446	55.95	55.19
$C_6H_5CH_2CH{=}CHCH_2OC_3H_7$.	55.8	23	99—100 (2mm)	1.5100	0.9381	60.66	59.81
$C_6H_5CH_2CH{=}CHCH_2OC_4H_9$.	43.1	18.5	103—104 (5mm)	1.5044	0.9249	65.00	64.43

As can be seen from the data in the table, the reaction rate of nucleophilic exchange of the halide for the alkoxy group in 2 is at least as great again as the rate of the splitting out of HCl. It is known that halogen derivatives of the allyl chloride or $RCH{=}CHCH_2Cl$ (where R = alkyl) type, when treated with alcoholic alkali, usually undergo only an exchange reaction, giving the corresponding ethers, as the lability of the chlorine atom here is increased due to the conjugation of the C-Cl bond with the double bond. In a (I) molecule in conjugation with the double bond, besides the chlorine atom, there is a phenyl radical which has an effect opposite to that of an alkyl radical. By attracting the electrons it thus makes the H-atom in position 1 labile, which to a large extent, favors the splitting out of hydrogen chloride elements from the (I) molecule.

If a substitutent with an electrophilic character is present in the benzene nucleus, then the displacement of the electrons towards the aryl radical is of such strength that only the splitting out of HCl occurs. Such a result is observed in the case of treatment of 4-chloro-1-(p-nitrophenyl)-butene-2 with alcoholic alkali [7]. As can be seen from the data in the table, the yields of both reaction products decrease when the alkyl radical becomes complicated by the addition of an alcohol molecule. 1-Phenyl-4-alkoxybutenes-2 are colorless liquids with a weak characteristic smell.

It should be noted that the molecular refraction of all four ethers obtained is 0.6–0.7 of a unit greater than that calculated due to the presence of a double bond conjugated with the benzene nucleus as well as the alkoxyl group.

Thus, it turned out that solutions of alcoholic alkali in this case are not suitable reagents for splitting off hydrogen chloride. Attempts to apply other known methods of splitting off hydrogen chloride, for example, by the action of quinoline, methyl- or dimethylaniline, pyridine and triethylamine, did not give positive results.

In all cases, complete resinification of the reaction mixture occurred. An acceleration of the polymerization of (II) in the presence of pyridine was noted in the article by one of us [3]. The reaction practically did not proceed in the cold or at room temperature.

After some searching we were able to develop a new practical method of preparing α-phenylbutadiene. Two methods were developed. In the first method (I) was added to a mixture of potassium hydroxide powder and dioxane in a four-fold amount (in relation to the chloride) and heated to boiling. The reaction proceeded with the evolution of heat and no further heating was required. The reaction of 0.2 mole of (I) was complete in 8–10 minutes. The reaction conditions were so mild that almost no resinification or polymerization of (II) was observed. The method was tested for amounts from 0.05 to 0.5 mole. The yields were 90%. The method developed could be the main way of preparing α-arylbutadienes from compounds of the 4-halo-1-arylbutene-2 type and other halogen derivatives of the aliphatic class of compounds.

In the second method (I) was added to potassium hydroxide powder in a Claisen flask. The reaction was carried out under reduced pressure. The (II) formed was immediately distilled.

The constants of the (II) obtained in both cases were similar to those of the **trans-isomer.**

EXPERIMENTAL

1-Phenyl-4-alkoxybutenes-2. 100 ml of 2 N (0.2 mole) solution of potassium hydroxide in the appropriate alcohol and 16.7 g (0.1 mole) of (I) were placed in a three-necked flask equipped with a stirrer, thermometer and reflux condenser. The mixture was stirred and heated. The reaction began at 40–50° and was indicated by turbidity and the deposition of potassium chloride. After heating (finally to boiling) for 1.5 hours, the mixture was diluted to double its amount with water. After extraction with ether, the ether extract was washed until neutral and dried with anhydrous magnesium sulfate. When the ether had been removed, the residue – a mixture of the unsaturated ether and (II) – was distilled in vacuum from a flask with a small fractionating column. The (II) was identified by its constants and the melting point of its adduct with maleic anhydride. The constants of the ethers are given in the table.

1-Phenyl-4-methoxybutene-2. By distilling the 16 g of liquid obtained from the reaction, the following fractions were isolated: a) 85–89° (11 mm), 3.4 g (26.1%) and b) 108–109° (11 mm), 10.8 g (66.7%).

Fraction "a" was (II) and had the following constants after a second distillation:

B.p. 85–87° (10 mm), n_D^{20} 1.5903, d_4^{20} 0.9270, MR_D 47.41. $C_{10}H_{10}F_5$ calc. 43.85.

Literature data: b.p. 78–81° (8 mm), n_D^{25} 1.6070 [4], b.p. 86° (11 mm), n_D^{28} 1.5950 [8].

Condensation of a sample of (II) with maleic anhydride by the usual method gave a crystalline adduct with m.p. 120° (from benzene). According to literature data the m.p. is 120° [9]. A mixed melting point did not show depression.

Fraction "b" was the ether 1-phenyl-4-methoxybutene-2.

Found %: C 81.75, 81.56; H 8.84, 8.76. $C_{11}H_{14}O$. Calculated %: C 81.44; H 8.70.

1-Phenyl-4-ethoxybutene-2. By distillation of the 15 g of oil obtained we isolated 3.3 g (25%) of (II) and 10 g (60%) of the ether, which was analyzed.

Found %: C 81.96, 81.98; H 9.36, 9.48. $C_{12}H_{16}O$. Calculated %: C 81.77; H 9.15.

1-Phenyl-4-n-propoxybutene-2. From the 15 g of reaction product obtained, we isolated 3 g (23%) of (II) and 10.60 g (55.8%) of the ether, which was analyzed.

Found %: C 81.97, 81.98; H 9.45, 9.50. $C_{13}H_{18}O$. Calculated %: C 82.06; H 9.54.

1-Phenyl-4-n-butoxybutene-2. From 14 g of reaction product we isolated 2.4 g (18.5%) of (II) and 8.8 g (43.1%) of the ether, which was analyzed.

Found %: C 82.36, 82.13; H 9.73, 9.78. $C_{14}H_{20}O$. Calculated %: C 82.30; H 9.87.

α-Phenylbutadiene (II). a) 45 g (0.8 mole) of powdered potassium hydroxide and 75 ml of anhydrous dioxane were placed in a three-necked flask equipped with a stirrer, reflux condenser and dropping funnel. The mixture was heated until the dioxane started to boil. 33.5 g (0.2 mole) of (I) was added from the funnel with the stirrer rotating slowly. No further heating was required as the reaction proceeded with the evolution of heat. (I) was added at such a rate that the mixture boiled gently. After all the chloride had been added, the contents of the flask were boiled for 2–3 minutes. The end of the reaction could readily be established by a Beilstein test. When cool, the reaction mixture was poured into 150 ml of water. The oil floating on top was extracted with 100 ml of ether. The extract was washed 2–3 times with water to a neutral reaction and, after adding a little hydroquinone, dried with calcium chloride. After distilling off the solvent, the residual liquid was distilled in vacuum. 23.5 g (90%) of (II) was distilled. B.p. 65–66°; (3 mm); 73–74° (10 mm); n_D^{20} 1.6073. The adduct with maleic anhydride had m.p. 120°.

b) The hydrogen chloride was split out from (I) in a vacuum distillation apparatus. 20 g (0.36 mole) of slightly moist powdered potassium hydroxide was placed in a flask with a small fractionating column, fitted with a thermometer and a dropping funnel in the place where the capillary is normally situated. The flask was immersed in an oil bath previously heated to 100–105° and 20 g (0.12 mole) of (I) was gradually added. At 60–65° and 3 mm a colorless, transparent liquid distilled off. When all the chloride had been added (about 10 minutes was required for this), the distillation was continued until (II) no longer distilled off. In the receiver we collected 12 g (about 80%) of pure (II). B.p. 62–65° (3 mm), n_D^{20} 1.5990. Organic chlorine was not present in the distillate. (II) was identified by the melting point of the adduct with maleic anhydride.

SUMMARY

1. The reaction of 4-chloro-1-phenylbutene-2 with solutions of potassium hydroxide in aliphatic alcohols resulted simultaneously in the formation of α-phenylbutadiene and the corresponding 1-phenyl-4-alkoxybutenes-2.

2. $C_6H_5CH_2CH{=}CHCH_2OAlk$, were obtained where $Alk{=}CH_3$, C_2H_5, $n\text{-}C_3H_7$ and $n\text{-}C_4H_9$.

3. A new method was developed for synthesizing α-phenylbutadiene by splitting out hydrogen chloride from 4-chloro-1-phenylbutene-2 with potassium hydroxide powder in dioxane or by distillation over potassium hydroxide in vacuum.

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THE HALOARYLATION OF UNSATURATED COMPOUNDS WITH AROMATIC DIAZO COMPOUNDS

IV. SYNTHESIS OF β-ARYLALKYL CARBOXYLIC ACIDS

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As previously reported [1], aromatic diazonium salts in presence of cupric chloride in aqueous acetone solution add on to acrylonitrile at the double bond to give α-chloro-β-arylpropionitriles in good yield.

Methyl acrylate (I) and methyl methacrylate (II) react similarly in presence of cupric chloride to form products of haloarylation.

$$ArN_2Cl + \underset{(I)}{CH_2{=}CH{-}COOCH_3} \xrightarrow{CuCl_2} ArCH_2{-}CHClCOOCH_3$$

$$ArN_2Cl + \underset{(II)}{CH_2{=}C(CH_3)COOCH_3} \xrightarrow{CuCl_2} ArCH_2{-}CCl(CH_3){-}COOCH_3$$

The reaction of methyl methacrylate with p-nitrophenyldiazonium chloride has already been described; however, the chemical properties of methyl-α-chloro-β-(4-nitrophenyl)-isobutyrate have not been studied. Haloarylation of acrylates (I) and (II) was performed by the procedure that we described in the preceding communication [1] with the sole difference that more drastic temperatures conditions were used: it was necessary to heat the mixture to 35-45°.

It was shown that at 44-50° diazotized α- and β-naphthylamines also react with acrylonitrile.

It must be pointed out that methyl-α-chloro-β-(4-nitrophenyl)-isobutyrate splits off a molecule of hydrogen chloride when treated with aqueous solutions of caustic alkali and at the same time is saponified to form α-methyl-β-(4-nitrophenyl)-acrylic acid. In this respect it behaves similarly to α-chloro-β-arylpropionitriles. Methyl-α-chloro-β-(4-nitrophenyl)-propionate, obtained from methyl methacrylate (I) and p-nitrophenyldiazonium salt, is converted into methyl 4- nitrocinnamate in 79% yield on heating with potassium phthalimide. Compounds prepared by the haloarylation reaction are listed in the table.

Both the α-chloro-β-arylpropionitriles and the methyl esters of α-chloro-β-arylisobutyric acids are of definite preparative interest.

In this communication we report the results of investigations of the transformations of the products of halophenylation and halonaphthylation into the corresponding β-substituted propionic and isobutyric acids, analogs of which have found application as plant-growth stimulators:

$$ArCH_2CHClCN \xrightarrow{Zn/CH_3COOH} ArCH_2CH_2CN,$$

$$ArCH_2CH_2CN \xrightarrow{H_2O} ArCH_2CH_2COOH,$$

$$ArCH_2{-}\overset{\displaystyle CH_3}{\underset{\displaystyle Cl}{C}}{-}COOCH_3 \xrightarrow{Zn/CH_3COOH} ArCH_2{-}\overset{\displaystyle CH_3}{CH}{-}COOH.$$

TABLE

Chlorophenyl and Chloronaphthyl Derivatives of Acrylonitrile, Methyl Acrylate and Methyl Methacrylate

Substance	Reaction temperature	% yield of substance	Constants of prepared substances
Methyl-α-chloro-β-(4-nitrophenyl)-propionate	25°	50	M. p. 38—40°
Methyl-α-chloro-β-phenylisobutyrate	27—29	50	B. p. 118—119° (10 mm)
Methyl-α-chloro-β-(4-nitrophenyl)-isobutyrate	27—30	72	M. p. 102.5—103.5°
α-Chloro-β-(1-naphthyl)-propionitrile	40	*	—
α-Chloro-β-(2-naphthyl)-propionitrile	50	*	—

* The prepared substances were reduced and saponified to the corresponding acids without purification.

We also utilized this reaction for the synthesis of naphthylpropionic acids. The chloronaphthyl derivatives of acrylonitrile were reduced with zinc in glacial acetic acid and after hydrolysis they were transformed into 2-(α-naphthyl)- and 2-(β-naphthyl)-propionic acids.

EXPERIMENTAL

Methyl α-chloro-β-phenylisobutyrate. Into a two-necked flask, fitted with stirrer and thermometer, were placed 20 g methyl methacrylate (II), 100 ml acetone, 5 g cupric chloride and a solution of phenyldiazonium salt prepared from 19.8 g aniline. The mixture was gently heated; nitrogen started to come off at 27-29° and ceased to come off after 2 hours. At this stage the reaction mass was diluted with water and the resultant oil was extracted with ether. The ethereal solution was dried, the solvent was driven off and the residue distilled in vacuum to give 19.55 g (47%) of a fraction with the constants:

B.p. 136-136.5° (15 mm), n_D^{20} 1.5154, d_4^{20} 1.151, MR_D 55.72. $C_{11}H_{13}O_2Cl\bar{}_3$. Calc. 56.28.

Found %: C 62.19, 62.34; H 6.09, 6.14; Cl 16.05, 16.01. $C_{11}H_{13}O_2Cl$. Calculated %: C 62.12; H 6.16; Cl 16.67.

Methyl α-chloro-β-(4-nitrophenyl)-isobutyrate. The same procedure and conditions as above were used for the reaction of a solution of 20 g methyl methacrylate (II) in acetone and p-nitrophenyldiazonium salt prepared from 27.5 g p-nitroaniline. Yield 37 g (72%) of isobutyrate with m. p. 102.5-103.5° [2].

β-Phenylpropionic acid. 9 g of α-chloro-β-phenylpropionitrile, prepared by the earlier procedure [1], was dissolved in 40 ml glacial acetic acid; the solution was transferred to a three-necked flask fitted with stirrer, reflux condenser and thermometer; portionwise addition was then made, with good stirring, of 10 g zinc dust. After the vigorous reaction had ceased, the mixture was heated 2 hours at 110°, the acetic acid solution was separated, 40 ml concentrated hydrochloric acid was added to it and the mixture refluxed for 8 hours. The solvents were removed in vacuum and the solid residue was extracted with hot benzene. Removal of the benzene left 4.0 g (49%) of acid with m.p. 47° (from methanol) [3].

β-Phenylisobutyric acid. Reduction of 5 g of methyl α-chloro-β-phenylisobutyrate by the procedure described above gave 2.5 g (65%) of acid with b.p. 135-137° (10 mm), m.p. 37° [4].

2-(α-Naphthyl)-propionic acid. From 8 g acrylonitrile, dissolved in 100 ml acetone, and α-naphthyldiazonium solution prepared from 21.5 g α-naphthylamine at 41-42°, was obtained an oil which without purification was subjected to further treatment, in a solution of 30 ml glacial acetic acid, with zinc dust (10 g) (4 hours at 110°). After separation from sludge, addition was made to the solution of an equal volume of concentrated hydrochloric acid and the mixture was refluxed for 3 hours. After cooling, 13.4 g (45%) of acid was obtained with m.p. 154-155° (from alcohol) [5].

2-(β-Naphthyl)-propionic acid. Using the above procedure, 5.4 g acrylonitrile in acetone and β-naphthyldiazonium, prepared from 14.3 g β-naphthylamine, gave after reduction and saponification 10 g (50%) acid with m.p. 135° [6].

α-Methyl-β-(4-nitrophenyl)-acrylic acid. A solution of 2.6 g methyl α-chloro-β-(4-nitrophenyl)-isobutyrate in 20 ml alcohol was refluxed in a flask with 2 g potassium hydroxide for 40 minutes. Yield 2 g (91%) acid with m.p. 207-208° (from glacial actic acid) [7].

Methyl α-chloro-β-(4-nitrophenyl)-propionate. A similar method was used for preparation from 8.6 g methyl acrylate and 13.5 g diazotized p-nitroaniline at 25° of 12.2 g (50%) propionate with m.p. 38-40°.

Found %: N 5.66. $C_{10}H_{10}O_4NCl$. Calculated %: N.5.79.

Methyl 4-nitrocinnamate. 3 g methyl α-chloro-β-(4-nitrophenyl)-propionate and 4 g potassium phthalimide were heated at 140-150° for 4 hours; 15 ml p-xylene was added and the hot solution was quickly filtered. The filtrate deposited 2 g (79%) yellow crystals of methyl 4-nitrocinnamate with m.p. 159.5-160.5° (from alcohol); m.p. 160.5° (micro determination) [8].

SUMMARY

1. Methyl acrylate and methyl methacrylate react with diazonium salts in aqueous acetone solution in presence of cupric chloride to give methyl esters of α-chloro-β-arylpropionic and α-chloro-β-arylisobutyric acid.

2. Reduction of α-chloro-β-phenylpropionitrile and methyl α-chloro-β-phenylisobutyrate with zinc in glacial acetic acid gave good yields of β-phenylpropionic, β-phenylisobutyric, 2-(α-napthyl)- and 2-(β-naphthyl)-propionic acids.

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THE NITRATION OF 1-n-BUTYLNAPHTHALENE

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In the present work the nitration of 1-n-butylnaphthalene* was investigated for the first time. Nitration was effected with nitric acid of various concentrations under various conditions. Preliminary experiments showed that: 1) nitration takes place only when using nitric acid containing oxides of nitrogen; 2) 1-butylnaphthalene nitrates completely with the help of nitric acid (d 1.4) at a temperature of −10°; in this way a liquid mixture of nitro compounds is formed whose main component is 4-nitro-1-butylnaphthalene; 3) the mixture of nitro compounds obtained cannot be resolved into its components merely by fractional distillation. Subsequently we employed the method of chromatographic adsorption in an attempt to obtain a closer insight into the composition of the mixtures obtained under various conditions; this method had not previously been applied to 1-alkylnitronaphthalenes. The adsorbent was aluminum oxide for chromatography (F-2); solvents used in succession were ligroin , benzene, chloroform and ethyl acetate. The material subjected to chromatography in the first experiments was the liquid mixture of nitro compounds obtained by nitrating with nitric acid at −10° and previously twice distilled (b.p. 144-147° at 1 mm). Chromatography yielded (experiment 1) 4-nitro-1 butylnaphthalene (its structure was confirmed by oxidation with nitric acid in a sealed tube to form 4-nitro-1-naphthoic acid) and a crystalline substance with m.p. 104°. The latter was isolated in such minute amount that it could not be investigated in more detail. Considerable resinification occurred when the mixture of nitro compounds was distilled, due to which a portion of the nitro compounds formed escaped observation. In all later experiments, the mixture of nitro compounds was therefore not distilled before chromatography. Chromatography of the undistilled mixture of nitro compounds, obtained under the conditions mentioned above, did not lead to new results; the composition of the mixture remained the same; nitration with nitric acid of the same composition but at +40° (experiment 2) led to higher yield of the crystalline substance; this enabled it to be purified and analyzed and its structure to be determined by means of an oxidation reaction. This compound was 4, 5-dinitro-1-butylnaphalene.. The same dinitro compound is the main product of reaction (yield 80%) in nitration of 1-butylnaphthalene with nitric acid (d 1.5) at −10° (experiment 3). Rise of temperature to +10° while using nitric acid of the same composition leads to a mixture of 4, 5-dinitro-1-butylnaphthalene (43%) with trinitrobutylnaphthalene (14.2%). The trinitro compound is best prepared from 1-butylnaphthalene by using nitric acid of d 1.5 at 20-30° or a mixture of nitric acid (d 1.5) and sulfuric acid (d 1.84) at −10° (experiment 5).

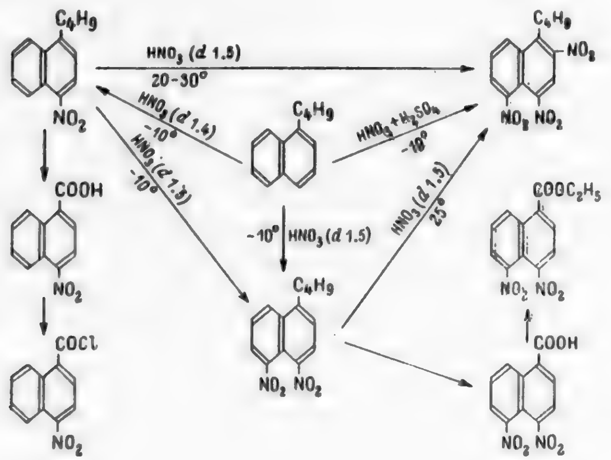
The experimental results showed that, depending upon the temperature and the nitric acid concentration, nitration of 1 butylnaphthalene gives mono-, di- and trinitro compounds in various ratios.

We utilized the qualitative reaction employed by Thompson [2] (in separating 1-methyl-2, 4-dinitronaphthalene and 1-methyldinitronaphthalene) for investigation of the products of nitration under conditions leading to formation of a dinitro compound side by side with trinitrobutylnaphthalene; the same reaction was also useful for evaluation of the completeness of separation of the compounds and to some extent also for elucidation of their structure. Thompson established that the only 1-methyldinitro compounds to give characteristic color reactions with aqueous acetonic or aqueous alcoholic solutions of ammonia or caustic soda are those containing one of the nitro groups in the 2 position of the naphthalene nucleus. Applying this reaction, we found that 4, 5-dinitro-1-butylnaphthalene does not give color reactions, and this fact was consistent both with our proposed

* Prepared by hydrogenation of 1-naphthylbutene-1 [1].

structure of the dinitro compound and with Thompson's observations. On adding to the test solutions in question, however, a mixture of 4, 5-dinitro-1-butylnaphthalene and trinitro compound, or the trinitrobutylnaphthalene alone, a definite coloration was observed. On the basis of these observations we may conclude that one of the nitro groups of 1-butyltrinitronaphthalene occupies the 2 position of the naphthalene nucleus. The position of the two other groups was established in further investigations in which both 4-nitro-1-butylnaphthalene and 4, 5-dinitro-1-butylnaphthalene were subjected to nitration under various conditions. The following results were then obtained: 4-nitro-1-butylnaphthalene is transformed almost completely into 4, 5-dinitro-1-butylnaphthalene by the action of nitric acid (d 1.5) at −10° (experiment 6); employment of nitric acid of lower concentration at various temperatures (from −10° to +10°) leads to only small amounts of dinitro compound (7-13%); rise of temperature in nitration with nitric acid of d 1.5 leads to formation of a mixture of dinitro and trinitro compounds; the trinitro compound becomes the main reaction product when nitration is effected at 20-30° (experiment 7). The trinitro compound was identical with the trinitro-1-butylnaphthalene obtained from 1-butylnaphthalene.

In the nitration of 4, 5-dinitro 1-butylnaphthalene we established the conditions (experiment 8) in which the sole product of reaction was the same as previously, namely trinitro-1-butylnaphthalene. Consecutive transformation of 1-butylnaphthalene into 4-nitro-1-butylnaphthalene, and 4, 5-dinitro-1-butylnaphthalene, and the transformation of 4, 5-dinitro 1-butylnaphthalene into trinitro-1-butylnaphthalene showed that in the latter the two nitro groups occupy positions 4 and 5 of the naphthalene nucleus. The position of the third group can, as indicated above, be established on the basis of Thompson's color reaction. The foregoing data enable us to conclude that the trinitro compound obtained in all the cases mentioned is 2, 4, 5-trinitro-1-butylnaphthalene. Moreover, the formation of the same polynitro compounds, regardless of the starting substance, indicates that nitro groups enter the naphthalene nucleus in a stepwise manner and always in the same order. The various transformations are represented by the following scheme:



EXPERIMENTAL

Nitration of 1-n-Butylnaphthalene

1. Nitration with nitric acid of d 1.4 at −10°; 4-nitro-1-butylnaphthalene. 20 g of 1-butylnaphthalene was added with rapid stirring in the course of 20 minutes at −10° to 40 ml nitric acid containing oxides of nitrogen. The reaction mixture was then stirred for 20 minutes and poured into water. The oily substance was extracted with ether and the ethereal extract was washed with water, with sodium carbonate solution and again with water. It was then dried with sodium sulfate. The ether was driven off to leave an oil which was distilled

in vacuum to give the following fractions: 1st fraction b.p. 99-110° (1 mm), 0.2 g; 2nd fraction b.p. 111-158° (1 mm), 23.1 g. The second fraction was redistilled to give: 1st fraction b.p. 99-101° (1 mm), 0.1 g (1-butylnaphthalene); 2nd fraction b.p. 102-142° (1 mm), 0.2 g; 3rd fraction b.p. 144-147° (1 mm), 20.5 g. The compound with b.p. 144-147° is a mixture of nitro compounds.

Chromatography of nitro compounds with b.p. 144-147° (1 mm)

a) Preparation of the column. A suspension of 60 g alumina for chromatography (F-2) in ligroin was poured in small portions into a tube with a diameter of 15 mm and a height of 1 meter. The solvent then flowed out uniformly from the tube and the alumina was deposited and became firm. After the whole of the alumina had been transferred to the tube, the upper layer of adsorbent was covered with a perforated porcelain plate and ligroin was poured over until a nonsettling column of sorbent was formed.

b) Chromatogramming. A solution of 3 g of twice-distilled substance with b.p. 144-147° (1 mm) in 30 ml ligroin (40-60° fraction) was passed through the column. After the whole of the solution had been taken up by the sorbent, the walls of the tube were washed with a small quantity of ligroin to remove traces of nitro product from the walls. After a short interval of time, the column was washed with ligroin, 30 ml lots of solution discharging from the column being collected (during the experiment the column of sorbent was continuously covered with liquid). Several fractions were obtained in this manner; the ligroin was driven off from them and the residue weighed and examined. Substances with similar properties were combined. Elution with ligroin was continued until no residue was detected after distillation of a fraction. After this, the column was eluted in succession with benzene, chloroform and ethyl acetate. Transition from one solution to another was effected gradually, increasing amounts of a second solvent being added to the first.* Chromatographic resolution of 3 g of mixture of nitro compounds gave 2.7 g of oily substance with b.p. 142-143° (1 mm) (from fractions obtained by elution of the column with ligroin), 0.05 g crystalline substance with m.p. 104° (from fractions collected during elution of the column with chloroform), 0.04 g intermediate fraction (obtained during elution with a mixture of benzene and chloroform) and 0.2 g resin. The compound with b.p. 142-143° (1 mm) is 1-butyl-4-nitronaphthalene; for analysis it was redistilled in vacuum: a light-yellow, viscous liquid with b.p. 132-133° (0.5 mm), odorless, soluble in benzene, chloroform, ether and acetone, insoluble in water or in solutions of acids and alkalies.

Found %: C 73.32; H 6.67; N 6.15. $C_{14}H_{15}O_2N$. Calculated %: C 73.34; H 6.59; N 6.11.

Oxidation of 4-nitro-1-butylnaphthalene purified by chromatography. 0.5 g 4-nitro-1-butylnaphthalene (b.p. 132-133° at 0.5 mm) and 5 ml of 11 % nitric acid solution were heated in a sealed tube at 180° for 8 hours. At the conclusion of the heating, the nitric acid was decanted and the residue (a crystalline substance admixed with resins) was treated with sodium carbonate solution. The solution was filtered and the filtrate was washed several times with ether and acidified with hydrochloric acid until acid to congo. The precipitated yellow crystals were collected and washed with water. Yield 0.1 g acid (25%) with m.p. 219-220°. After recrystallization from alcohol the m.p. was 222-223°. A mixture with 1, 4-nitronaphthoic acid (m.p. 223-223.5°) melted at 222-223°.

2. Nitration of 1-butylnaphthalene with nitric acid (d 1.40) at 40°; 4, 5-dinitro-1-butylnaphthalene. To 5 ml nitric acid (d 1.4) at +40° was added 2.5 g 1-butylnaphthalene; the mixture was stirred for 15 minutes at the same temperature and the reaction mass poured into water. Further working up was the same as in the preceding experiment. Yield 3.2 g oily substance, 3 g of which was subjected to chromatographic treatment as in experiment 1. The solvents, used in succession, were ligroin, benzene, dichloroethane, ethyl acetate and alcohol. Chromatography gave 2.55 g of 4-nitro-1-butylnaphthalene (from fractions obtained by elution of the column with ethyl acetate) with m.p. 104°. After two crystallizations from alcohol, the m.p. was 106.5-107°; light-yellow needles, soluble in benzene, chloroform and ethyl acetate, poorly soluble in gasoline, and ether, insoluble in water and in solutions of caustic alkalies and mineral acids. The substance does not give a coloration with aqueous alcoholic or aqueous acetonic solutions of sodium hydroxide or ammonia. On the basis of the elementary analysis the substance is dinitro-1-butylnaphthalene.

* All later chromatographic experiments were performed by this procedure.

Found %: C 61.42, 61.34; H 5.26, 5.07; N 10.15. $C_{14}H_{14}O_4N_2$. Calculated %: C 61.31; H 5.14; N 10.21

Oxidation of 4, 5-dinitro-1-butylnaphthalene. A mixture of 1 g dinitro-butylnaphthalene (m.p. 106.5-107°) with 15 ml 17% nitric acid solution was heated in a sealed tube for 7 hours at 175-178°. At the conclusion of the heating, the yellow crystals were filtered and dissolved in saturated sodium carbonate solution. Further treatment was the same as in the experiment on oxidation of 4-nitro-1-butylnaphthalene. Yield 0.5 g substance with m.p. 258°; after recrystallization from aqueous alcohol the substance has m.p. 264-265°; according to the literature [3] this is the melting point of 4, 5-dinitro-1-naphthoic acid.

Found %: N 10.60. $C_{11}H_6O_6N_2$. Calculated %: N 10.68.

The ethyl ester of 4, 5-dinitro-1-naphthoic acid was obtained by saturation with hydrogen chloride of a solution of the prepared 4, 5-dinitro-1-naphthoic acid in anhydrous ethyl alcohol. Yellow needles from alcohol, m.p. 142-143° (the literature reports m.p. 143° [3]).

3. Nitration of 1-butylnaphthalene with nitric acid (d 1.50) at −10°; 4, 5-dinitro-1-butylnaphthalene. To 3 ml fuming nitric acid at −10° was added 1.5 g 1-butylnaphthalene and the reaction mixture was stirred at the same temperature for 15 minutes and then poured into water; the oily substance was extracted with benzene. The benzene solution was washed with water, then with sodium carbonate solution and again with water; it was then dried with calcium chloride. After driving off the benzene, 2.1 g of oily substance was obtained; 2 g of this was chromatogrammed in a column containing 40 g alumina, using carbon tetrachloride as the first solvent, followed by ethyl acetate. Elution of the column with carbon tetrachloride gave 0.1 g of a mixture of 4-nitro-1-butylnaphthalene with 4, 5-dinitro-1-butylnaphthalene and 1.7 g of unpurified 4, 5-dinitro-1-butylnaphthalene with m.p. 104° (yield 80%); after recrystallization from alcohol the 4, 5-dinitro-1-butylnaphthalene melted at 106.5-107°. A mixed specimen with 4, 5-dinitro-1-butylnaphthalene from the preceding experiment melted at 106°.

Final washing of the adsorbent with ethyl acetate gave 0.2 g resin.

4. Nitration of 1-butylnaphthalene with nitric acid (d 1.50) at +10°; 2, 4, 5-trinitro-1-butylnaphthalene. To 1.5 ml nitric acid (d 1.50) was added 0.7 g 1-butylnaphthalene at +10°, and the mixture was stirred for 15 minutes and poured into water. The product was worked up as in the preceding experiments. Yield 1.1 g oily substance which solidified on standing: 1 g of this substance was subjected to chromatography from benzene, which gave 0.26 g of 4, 5-dinitro-1-butylnaphthalene with m.p. 104° (after recrystallization from alcohol the m.p. rose to 106°) and 0.49 g yellow crystalline substance with m.p. 85-86°. A mixture of this substance with 4, 5-dinitro-butylnaphthalene (m.p. 106.5-107°) melted at 92-93°. A deep color was developed when small amounts of the substance were added to an aqueous alcoholic or an aqueous acetonic solution of sodium hydroxide or ammonia.

Thus, the following colors were obtained when using solutions from 1 ml of 2 N aqueous NaOH or 2 N NH_4OH and 10 ml alcohol or acetone: NaOH + alcohol − red; NaOH + acetone − crimson; NaOH + alcohol − violet (develops gradually); NH_4OH + acetone − violet.

0.4 g substance with m.p. 85-86° was again chromatogrammed from benzene. This treatment gave 0.15 g of 4, 5-dinitro-1-butylnaphthalene (m.p. 104°, after recrystallization m.p. 106.5-107°), 0.16 g substance with m.p. 129-130° (after recrystallization from carbon tetrachloride m.p. 130°) and 0.08 g substance with m.p. 85-86°. A mixture of the substance with m.p. 130° and 4, 5-dinitro-1-butylnaphthalene (m.p. 106.5-107°) melted at 85-86°. The substance with m.p. 130° gives color reactions.

Using solutions of 1 ml 2 N aqueous NaOH or NH_4OH and 10 ml alcohol or acetone, the following colors were obtained: NaOH + alcohol − red; NaOH + acetone − cherry-red; NH_4OH + alcohol − pink; NH_4OH + acetone − violet.

The substance with m.p. 130° forms long, yellow needles (from carbon tetrachloride), readily soluble in benzene, chloroform and ethyl acetate, less soluble in alcohol and carbon tetrachloride, and insoluble in water, gasoline and solutions of caustic alkalies and mineral acids. Judging by the elementary analysis, the substance is trinitrobutylnaphthalene.

Found %: C 53.11; H 4.24; N 13.48. $C_{14}H_{13}O_6N_3$. Calculated %: C 52.66; H 4.10; N 13.15.

Performance of the reaction by the same method but at a temperature of 20° gave trinitro-1-butylnaptha-lene in a yield of 67%.

5. Nitration of 1-butylnaphthalene with a mixture of sulfuric and nitric acids at −10°; 2, 4, 5-trinitro-1-butylnapthalene. To a mixture of 0.75 ml nitric acid (d 1.5) and 0.75 ml sulfuric acid (d 1.84) was added 1 g 1-butylnaphthalene with vigorous stirring. The temperature of the mixture was held at −10° during this operation. The reaction mixture was thereupon stirred for a further 10-15 minutes before pouring into iced water. The product was worked up as in the preceding experiment. Yield 1.57 g oily substance. This solidified on standing; 1 g of this substance was chromatogrammed in a column containing 20 g alumina, using the following solvents in succession: benzene, chloroform, carbon tetrachloride, ethyl acetate and alcohol. Elution of the column with benzene gave 0.82 g crystals with m.p. 130°. The compound gives the color reactions characteristic of 2, 4, 5-trinitro-1-butylnaphthalene. A mixture with the previously obtained trinitrobutylnaphthalene (m.p. 130°) melted at 130°. (Yield of trinitrobutylnaphthalene 73.9%, reckoned on the 1-butylnaphthalene.)

No desorption of substance was effected in subsequent elution of the column with chloroform, carbon tetrachloride and ethyl acetate. Final elution of the column with ethyl alcohol gave 0.18 g of resin.

Nitration of 4-Nitro-1-Butylnaphthalene

6. Nitration with nitric acid (d 1.5) at −10°; 4, 5-dinitro-1-butylnaphthalene. With vigorous stirring at −10°, 2 g 4-nitro-1-butylnaphthalene was added to 4 ml nitric acid (d 1.5); stirring was then continued for another 10 minutes, after which the reaction mixture was poured into iced water. The oily substance was extracted with benzene and the benzene solution was washed with water until neutral and dried with calcium chloride. Removal of the benzene left 2.5 g oily product; 2 g of this was chromatogrammed in a column containing 40 g alumina, using the following solvents in succession: benzene, chloroform, carbon tetrachloride, ethyl acetate and alcohol. Elution of the column with benzene gave 0.13 g of original 4-nitro-1-butylnaphthalene, then 0.08 g of a mixture of the original substance with 4, 5-dinitro-1-butylnaphthalene; further washing of the column with the same solvent gave 1.7 g (91.3%) 4, 5-dinitro-1-butylnaphthalene with m.p. 104°. After recrystallization from alcohol the m.p. was 106.5-107°. A specimen of this compound mixed with 4, 5-dinitro-1-butylnaphthalene (m.p. 106.5-107°) isolated during nitration of 1-butylnaphthalene melted at 106°. No desorption of substance occurred in subsequent elution of the column with chloroform, carbon tetrachloride and ethyl acetate. Final washing of the column with alcohol gave 0.1 g resin.

7. Nitration of 4-nitro-1-butylnaphthalene with nitric acid (d 1.5) at 20-30°; 2, 4, 5-trinitro-1-butylnaphthalene. To 3.5 ml nitric acid (d 1.5) was added 1.5 g 4-nitro-1-butylnaphthalene at 20-30°; stirring was then continued for 10 minutes at the same temperature before the mass was poured into water. The product was worked up as in the preceding experiments. 1.85 g of oily substance was obtained and crystallized on standing. 1.5 g was subjected to chromatographic resolution from benzene to give 1.11 g compound with m.p. 129-130° (130° after recrystallization from carbon tetrachloride). A mixture with trinitrobutylnaphthalene prepared from 1-butylnaphthalene also melted at 130°.

8. Nitration of 1-butyl-4, 5-dinitronaphthalene with nitric acid (d 1.5) at +25°. To 3 ml nitric acid (d 1.5) was added 1 g 4, 5-dinitro-1-butylnaphthalene at +25°. The mixture was stirred for 10 minutes and poured into water. The oily substance was extracted with benzene and worked up as in the preceding experiments to give 1.1 g oily substance which crystallized on standing; 1 g of this was chromatogrammed; solvents: carbon tetrachloride and ethyl acetate.

Chromatographic separation yielded 0.7 g trinitrobutylnapthalene with m.p. 129-130° (130° after recrystallization from benzene). A mixture with trinitrobutylnapthalene (m.p. 130°), prepared by nitration of 1-butylnaphthalene and 4-nitro 1-butylnaphthalene, melted at 130°.

SUMMARY

1. Nitration of 1-n-butylnaphthalene, 4-nitro-1-n-butylnaphthalene and 4, 5-dinitro-1-n-butylnaphthalene was effected under various conditions.

2. Chromatographic adsorption was employed for resolution of the mixture of nitro compounds obtained by nitration.

3. The structure of 4-nitro-1-n-butylnaphthalene and 4, 5-dinitro-1-n-butylnaphthalene was confirmed, and the position of two nitro groups in trinitro-1-n-butylnaphthalene was established. The position of the third nitro group in trinitrobutylnaphthalene was predicted.

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4-AMINO-1-n-BUTYLNAPHTHALENE AND ITS TRANSFORMATIONS

S. I. Sergievskaya and T. S. Safonova

We prepared 4-amino-n-butylnaphthalene by catalytic reduction of 4-nitro-1-n-butylnaphthalene in presence of skeletal nickel catalyst.

4-Amino-1-n-butylnaphthalene is a liquid which darkens rapidly in the air especially when heated; its distillation was therefore effected in a nitrogen atmosphere and in presence of antioxidants. 4-Nitro-1-n-butylnaphthalene purified only by distillation can be taken for the reduction; as we have previously noted [1], this material contains a small amount of 4, 5-dinitro-1-n-butylnaphthalene; the sole reaction product that we isolated was then 4-amino-1-n-butylnaphthalene, but its purification was more difficult.

For the preparation of derivatives of aminobutylnaphthalene substituted at the amino group, it is very much more convenient to start from 4-nitro-1-n-butylnaphthalene purified by chromatography, and then to subject the reduced product without distillation to further transformations. We used 4-amino-1-n-butylnaphthalene for the preparation of 4-chloro- and 4-iodo-1-n-butylnaphthalene via a diazo compound. Diazotization of aminobutylnaphthalene is complicated by the poor solubility of its hydrochloride and sulfate in acids. During replacement of the diazo group by halogen, it was found that relatively facile deamination occurs at the same time as formation of halo or hydroxy compounds; thus in the preparation of 4-chloro-1-n-butylnapthalene by the action of cuprous chloride on the diazo compound, we obtained 1-n-butylnaphthalene in 27.9% yield in addition to 4-chloro- and 4-hydroxy-1-butylnaphthalene. Deamination did not occur when the diazo group was replaced by iodine with the help of an equivalent amount of potassium iodide in sulfuric acid solution, and only 4-iodo- and 4-hydroxy-1-n-butylnaphthalene were isolated. If, however, an excess of potassium iodide (1.5 moles) were used, then 1-n-butylnaphthalene is formed in addition in a yield of about 10%.

We prepared 4-n-butyl-1-naphthoic acid from 4-iodo-n-butylnaphthalene by the Grignard reaction.

EXPERIMENTAL

4-Amino-1-n-butylnaphthalene. To a solution of 4.5 g 4-nitro-1-n-butylnaphthalene (b.p. 132-133° at 0.5 mm) in 90 ml of a 2 : 1 mixture of ethyl acetate and alcohol was added 1 g skeletal nickel catalyst and hydrogenation was effected at atmospheric pressure and a temperature of 35-40°. In the course of 30 minutes the theoretical amount of hydrogen (1320 ml) was absorbed. After working up in the usual manner and removal of the solvent, the residual substance was dissolved in ether and dried with potassium carbonate. After the ether had been driven off, the substance was distilled in vacuum in a nitrogen stream with addition of a small quantity (0.1%) of ethyl 2-mercapto-4-aminobenzoate. Yield 3.6 g (88%) of 4-amino-1-n-butylnaphthalene with b.p. 141-142° (1 mm). The compound was redistilled for analysis; b.p. 133.5-134° (0.5 mm).

4-Amino-1-n-butylnaphthalene is a pale-yellow, oily substance rapidly darkening in the air, soluble in the majority of organic solvents, sparingly soluble in mineral acids, insoluble in water and caustic alkali.

Found %: C 84.02; H 8.40; N6.56. $C_{14}H_{17}N$. Calculated %: C 84.37; H 8.60; N 7.02.

4-Amino-1-butylnaphthalene hydrochloride forms colorless plates from alcohol, m.p. 229-231° (decomp.), soluble in alcohol, hot benzene, ethyl acetate, sparingly soluble in solutions of mineral acids, insoluble in ether, acetone and water.

Found %: N 6.09; Cl 15.27. $C_{14}H_{17}N \cdot HCl$. Calculated %: N 5.94; Cl 15.09.

4-Acetylamino-1-n-butylnaphthalene was prepared by the action of 0.3 ml acetic anhydride on a solution of 0.5 g 4-amino-1-butylnaphthalene in 1 ml benzene. The colorless crystals were recrystallized from benzene. Yield 0.57 g (93.4%) with m.p. 129-130°.

For analytical purposes the compound was twice recrystallized from benzene. Colorless needles, m.p. 131-131.5°; soluble in alcohol, acetone and other organic solvents, insoluble in water and solutions of acids and alkalies.

Found %: N 5.74. $C_{16}H_{19}ON$. Calculated %: N 5.80.

4-Acetylamino-1-n-butylnaphthalene was also prepared by another method. To a solution of 2.6 g 4-nitro-1-butylnaphthalene (b.p. 132-133° at 0.5 mm), isolated by chromatography, in 30 ml alcohol was added 1 g skeletal nickel catalyst, and the mixture was shaken in a hydrogen atmosphere at 35-40° and atmospheric pressure. In the course of 25 minutes 760 ml hydrogen was absorbed. After working up in the usual manner and removal of the alcohol, 6 ml anhydrous benzene and 2 ml acetic anhydride were added to the residue (2.2 g). 2.58 g product was obtained with m.p. 127-129°, rising to 131-137° after recrystallization from benzene. In order to check the individuality of the substance with m.p. 127-129°, 1 g of this was chromatogrammed over alumina, using benzene as solvent. This operation yielded only one substance (0.91 g) with m.p. 129-130°; after recrystallization from benzene m.p. 131-131.5°. A mixture of this substance with the 4-acetylamino-1-butylnaphthalene (m.p. 131-131.5°) prepared in the preceding experiment melted at 130-131°.

4-Benzoylamino-1-n-butylnaphthalene. To a solution of 1 g 1-butyl-4-aminonaphthalene in 5 ml anhydrous benzene was added 0.8 ml benzoyl chloride. The crystalline precipitate was washed several times with ether. Yield 1.35 g (88%) substance with m.p. 129-130°, rising to 132-132.5° after two recrystallizations from alcohol. Long colorless needles, soluble in acetone, hot benzene and chloroform, insoluble in water and in solutions of mineral acids and alkalies.

Found %: N 4.70, 4.72. $C_{21}H_{21}ON$. Calculated %: N 4.61.

4-Chloro-1-n-butylnaphthalene. To 10 g 4-amino-1-butylnaphthalene in 100 ml 28% hydrochloric acid was added a solution of 3.3 g sodium nitrite in 10 ml water (10% excess) at a temperature of −5 to 0°. The reaction mixture was stirred for 10 minutes at 0°, after which the excess of nitrous acid was removed by addition of urea. The solution of diazonium salt was rapidly filtered and added to a cooled (0°), freshly prepared solution of 5 g cuprous chloride in 50 ml concentrated hydrochloric acid. The mixture was heated to 90° and then cooled to room temperature. The resultant oily substance was extracted with ether and the ethereal solution was washed with 10% alkali solution and then with water (until neutral to litmus) and dried with calcium chloride. After the ether had been driven off, the residue was subjected to repeated fractional distillation in vacuum to give 3.7 g (33.7%) 4-chloro-1-butylnaphthalene and 2.6 g (27.9%) 1-n-butylnaphthalene.

4-Chloro-1-n-butylnaphthalene is a light-yellow liquid with b.p. 122.5-123° (1 mm), darkening in the air, soluble in the majority of organic solvents, insoluble in water.

Found %: Cl 15.82. $C_{14}H_{15}Cl$. Calculated %: Cl 16.21.

0.9 g (9%) 4-hydroxy-1-butylnaphthalene with b.p. 184-186° (9 mm) was obtained from the alkaline solution obtained by washing the ethereal extract, after acidification with hydrochloric acid and further working-up.

4-Iodo-1-n-butylnaphthalene. 10 g 4-amino-1-butylnaphthalene was dissolved with heating in 110 ml of 2 N sulfuric acid solution, then cooled to 0°, and a solution of 3.3 g sodium nitrite in 8 ml water was added with energetic stirring. The reaction mixture was stirred for 10 minutes, an aqueous solution of 8.3 g potassium iodide was added, and stirring was continued for 2 hours at room temperature. The solution was heated to 100° and then cooled. The resultant oil was extracted with benzene; the benzene solution was washed several times with warm sodium bisulfite solution, with 10% sodium hydroxide solution and with water (until neutral to litmus), and then dried with calcium chloride. After distillation of the benzene, the residual substance (9.8 g) was distilled in vacuum. Three distillations gave 7.6 g (49.5%) of 4-iodo-1-n-butylnaphthalene with b.p. 154-155° (1 mm).

4-Iodo-1-n-butylnaphthalene is a yellow oil, soluble in the majority of organic solvents, insoluble in water, rapidly breaking down with liberation of iodine.

Found %: C 54.47; H 5.03. $C_{16}H_{15}I$. Calculated %: C 54.21; H 4.87.

The alkaline solution obtained in washing the benzene solution gave, after acidification and the usual working-up, 1.1 g of 4-hydroxy-1-n-butylnapthalene with b.p. 184-185° (1 mm).

4-n-Butyl-1-naphthoic acid. To a mixture of 0.24 g magnesium and 50 ml absolute ether was added 0.1 ml methyl iodide and a solution of 3.1 g 4-iodo-1-n-butylnaphthalene in 10 ml absolute ether; the reaction mixture was stirred for 30 minutes at the boiling point of ether. After the magnesium had dissolved, the reaction mixture was poured into a mixture of absolute ether and solid carbon dioxide. The ether was decanted and the residue carefully triturated with 3 ml of 18% hydrochloric acid. Yield 1.14 g (50%) amorphous substance with m.p. 146-147°. After 2 recrystallizations from aqueous alcohol, 4-n-butyl-1-naphthoic acid melted at 148-148.5°. It was identical with the 4-n-butyl-1-naphthoic acid that we prepared from 1-n-butyl hydroxymethylnaphthalene.

SUMMARY

[1] 4-Amino-1-n-butylnaphthalene and its hydrochloride and acetyl and benzoyl derivatives were prepared.

[2] 4-Chloro-1-n-butylnaphthalene, 4-iodo-1-n-butylnaphthalene and 4-n-butyl-1-napthoic acid were prepared.

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THIAZOLIDINE-4-CARBOXYLIC ACID AND ITS DERIVATIVES

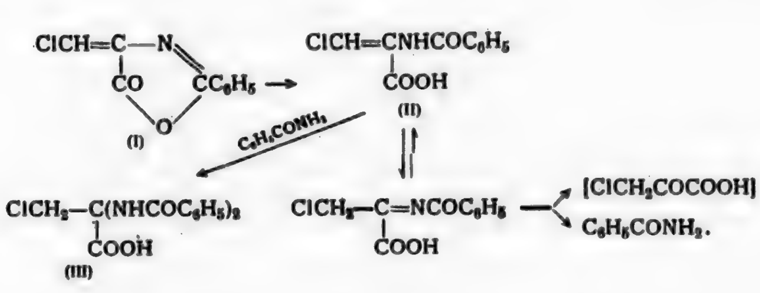
VII. STUDY OF THE PRODUCTS OF CONDENSATION OF α-AMINO-β-MERCAPTOACIDS WITH 4-CHLOROMETHYLENE-2-PHENYL-5-OXAZOLONE AND ITS DERIVATIVES

N. T. Strukov

4-Chloromethylene-2-phenyl-5-oxazolone has scarely been studied although its transformations are of great interest. It has been prepared by heating 4-hydroxymethylene-2-phenyl-5-oxazolone with thionyl chloride [1] as well as with phosphorus pentachloride. O. V. Kildisheva, L. P. Rasteikene and I. L. Knunyants found a new method of preparation of derivatives of this series which consisted in heating α, β-dihalo-α-acylaminopropionic acids with acetic anhydride. This method was applied to the preparation of 4-chloro-methylene- and 4-bromo-methylene-2-benzyl-5-oxazolones [2].

Our objective was to study the transformations of 4-chloromethylene-2-phenyl-5-oxazolone (I), and we found that in some cases the azlactone ring enters into reaction with much greater facility than the chlorine atom or the chloromethylene group. Under the action of an aqueous alcoholic solution of ammonia, the azlactone is converted into the amide of α-benzoylamino-β-chloro-acrylic acid. A 1 N solution of sodium hydroxide splits the azlactone ring with formation of the sodium salt of α-benzoylamino-β-chloroacrylic acid. Prolonged treatment of α-benzoylamino-β-chloroacrylic acid (II) with 1 N sodium hydroxide leads to benzamide and α-dibenzoylamino-β-chloropropionic acid (III). This reaction can be attributed to a tautomeric transformation of α-benzoylamino-β-chloroacrylic acid followed by hydrolysis to chloropyroracemic acid and benzamide. Benzamide then enters into reaction with still unchanged α-benzoylamino-β-chloroacrylic acid and evidently forms α, α-dibenzoylamino-β-chloropropionic acid (scheme 1).

Scheme 1



This reaction has much in common with the condensation of pyroracemic acid with two molecules of acetamide, when both acetylamino groups are in the α-position [3, 4].

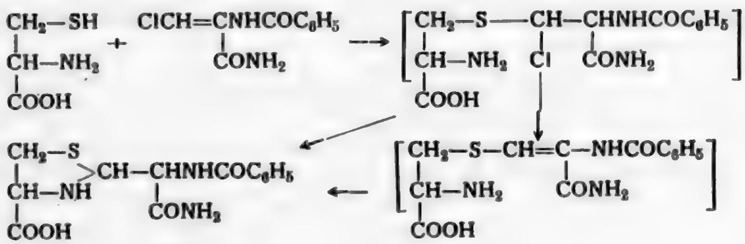
To what extent the chlorine atom in the β-position can change the order of addition of acid amides to the double bond has not been accurately established.

Oxidation of α-benzoylamino-β-chloroacrylic acid with 0.1 N potassium permanganate solution at room temperature in presence of sodium bicarbonate yielded oxalic acid in the form of the insoluble calcium salt and benzamide.

The difference in reactivity of the azlactone ring and the chloromethylene group in 4-choromethylene-2-phenyl-5-oxazolone was of interest in connection with their subsequent utilization in reaction with the amino and mercapto groups of penicillamine.

Dimethylacrylic acid and some of its derivatives are known to add on hydrogen sulfide [5], mercaptans [6] and thioacids [7] at the double bond. Acrylic and α-acetylaminoacrylic acids react with cysteine [8]. Addition goes in such a manner that the hydrogen of the mercapto group enters the α- and the remainder of the molecule the β-position.

α-Benzoylamino-β-chloroacrylamide was condensed with cysteine in presence of 1 N sodium hydroxide solution with the objective of establishing the ability of the double bond to add on mercapto compounds. After disappearance of the reaction for the mercapto group, the α-amide of desdimethylphenyl-penicilloic acid (IV), previously described by us [9], was isolated. The mechanism of the reaction is not quite clear; it is uncertain whether the mercapto group adds on at the double bond, hydrogen chloride splits off and the ring closes, or whether the addition of the mercapto group is followed by immediate reaction of a chlorine atom with a hydrogen of the amino group.



(IV)

It may be suggested that the chlorine in α-benzoylamino-β-chloroacrylamide at once exchanges with the cysteine group, but in that event it should possess fairly high mobility and be easily replaced by the hydroxy and amino group. Much more probable is the addition of the mercapto group to the double bond which also leads to activation of the chlorine and its cleavage in the form of hydrogen chloride.

This reaction prompted us to effect the synthesis of 1-thia-3-benzoyl-amino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid, which is of great interest for the preparation of compounds containing the thiazolidine-β-lactam system.

Previous work has been undertaken on the synthesis of compounds with a bicyclic thiazolidine-β-lactam system from acetals of some N-(penaldyl)-penicillamines. Attempts were made, in particular, to synthesize penicillins from acetals of N-(benzylpenaldyl)-penicillamine [10] and N-(amylpenaldyl)-penicillamine [11].

The methyl ester of N-methoxymethylene-phenaceturyl penicillamine is described in a monograph on penicillin [10]. When this ester was heated in ethereal solution it was transformed into a compound of unclarified structure. Possible structures proposed are those of methyl esters of 1-thia-2-methoxy-3-phenacetylamino-4-keto-5-aza-7, 7-dimethylcycloheptane-6-carboxylic acid and of 1-thia-2-methoxy-methyl-2-phenacetylamino-3-keto-4-aza-6, 6-dimethylcyclohexane-5-carboxylic acid.

A paper was recently published by I. L. Knunyants, O. V. Kildisheva and M. G. Linkova who showed that N-acrylyl-penicillamines in presence of caustic alkali add on the mercapto group intramolecularly to the $CH_2=CH$-bond to form 1-thia-4-keto-5-aza-7, 7-dimethyl-cycloheptane-6-carboxylic acid [12]. The same authors showed that under the action of caustic alkali the methyl ester of N-β-(chloroacrylyl)-penicillamine forms the

methyl ester of 1-thia-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid [12].

Evidently also in the event of closure of the seven-membered ring the same law of addition of the mercapto group to the ClCH=C-bond holds good, the chlorine being split off in the form of hydrogen chloride.

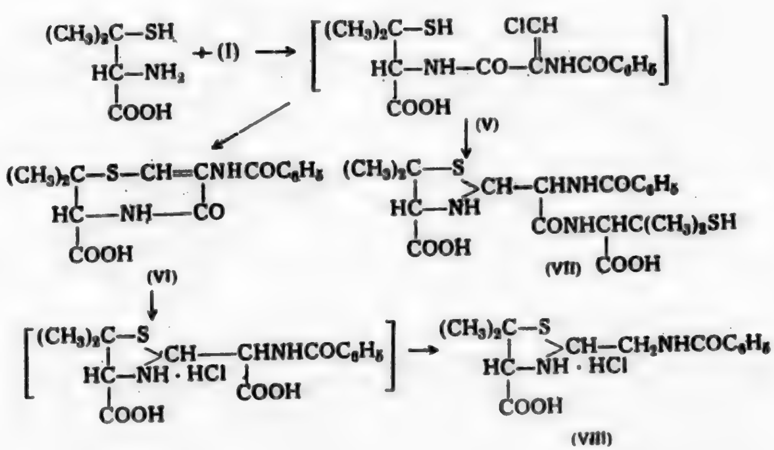
Finally, O. Süs has attempted to synthesize benzylpenicillin from N-phenaceturylpenicillamine and ethyl orthoformate. The author succeeded in obtaining a compound, in impure form for which he proposed the formula of 1 thia-3-phenacetylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid [13]. The structure of the compound was not verified.

We started our own investigations by preparing simpler model substances with an unsaturated seven-membered ring, with the objective of first studying its chemical properties before undertaking the synthesis and study of more complex and less accessible compounds of this series. 4-Chloromethylene-2-phenyl-5-oxazolone was most suitable for this purpose, since unlike 4-ethoxymethylene- and 4-aminomethylene-2-phenyl-5-oxazolones the chlorine atom in 4-chloromethylene-2-phenyl-5-oxazolone exerted a marked influence on the reduction of stability of the azlactone ring. This circumstance enabled the realization of the synthesis of a peptide bond that did not appreciably affect the function of the chlorine or of the chloromethylene group. On the other hand, from an experiment on condensation of cysteine with α-benzoylamino-β-chloroacrylamide we were aware of the behavior of the mercapto group towards the ClCH=C- bond. For this reason we considered that the synthesis of 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid was feasible.

Condensation of 4-chloromethylene-2-phenyl-5-oxazolone with penicillamine was carried out in presence of sodium hydroxide, as was done in the synthesis of peptides from amino acids and azlactones [14, 15]. Two substances were obtained: one of them was free from amino and mercapto groups and chlorine, was not oxidized by iodine solution, did not dissolve in dilute mineral acids, and corresponded in elementary composition to 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid (VI); the other was already soluble in acids and rapidly oxidized by iodine solution; this was the α-penicillamide of phenylpenicilloic acid (VII).

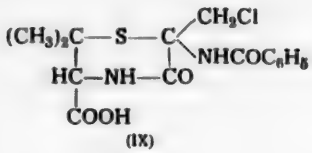
Formation of these compounds can be formulated fairly easily. In the condensation of the sodium salt of penicillamine with 4-chloromethylene-2-phenyl-5-oxazolone, an intermediate product is the sodium salt of N-(α-benzoylamino-β-chloroacrylyl)-penicillamine (V) which can react in two directions: intramolecularly with closure of the seven-membered ring (VI), and with a second molecule of sodium salt of penicillamine to form compound (VII) (scheme 2).

Scheme 2



These two substances were separated both by heating with a large volume of hot water, in which 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid is nearly insoluble, and with the help of dilute hydrochloric acid with which the α-penicillamide of phenylpenicilloic acid gives a readily soluble salt. The second method, however, is preferable because it enables the separation to be effected in the liquid phase.

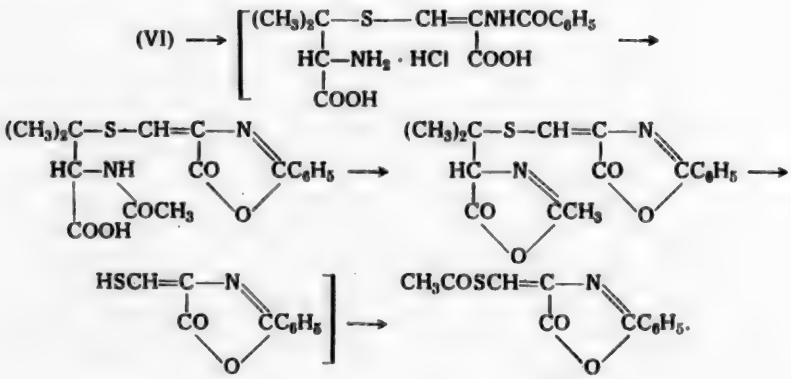
The main proof of the structure of 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid is provided by its cleavage at the peptide bond when heated with formic acid saturated with hydrogen chloride. This reaction led to the hydrochloride of phenylpenicilloic acid (VIII), which is described in the literature [16]. The process is accompanied by release of carbon dioxide. If the condensation of pencillamine with 4-chloromethylene-2-phenyl- 5-oxazolone had led not to 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid (VI) but to 1-thia-2-chloromethyl-2-benzoylamino-3-keto-4-aza-6, 6-dimethyl-cyclohexane-5-carboxylic acid (IX),



(IX)

as the result of a different order of addition of the mercapto group to the double bond, then its cleavage at the ring amido group could not have led to formation of the hydrochloride of phenylpenicilloic acid.

Careful cleavage of compound (VI) with concentrated hydrochloric acid at room temperature and subsequent azlactonization of the dry substance with acetic anhydride gave a small amount of the previously known 4-acetothio-methylene-2-phenyl-5-oxazolone (X) [17].



(X)

Careful oxidation of 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid with 0.1 N potassium permanganate solution at room termperature in presence of sodium bicarbonate gave benzamide, while subsequent acid cleavage of the amide bond gave oxalic acid which was isolated in the form of the calcium salt. These properties are in harmony with the structure of 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid, since oxidation in the first instance must involve S-CH=C grouping. Oxidation at once gives benzamide, but the oxalic acid still remains linked with the amino group and is only split off on heating with hydrochloric acid.

$$(VI) \rightarrow C_6H_5CONH_2 + \left[\begin{array}{ll} (CH_3)_2C{-}X & COOH \\ \quad HC & {-}NHCO \\ \quad COOH & \end{array}\right] \rightarrow \left[\begin{array}{l} (CH_3)_2C{-}X \\ \quad HC{-}NH_2 \\ \quad COOH \end{array}\right] + \begin{array}{l} COOH \\ | \\ COOH. \end{array}$$

X — oxidizable S−CHOH group.

Ammonia is released and benzoic acid formed when 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid is heated with a 1 N solution of sodium hydroxide, while heating with alcoholic hydrochloric acid leads to the ethyl ester of benzoic acid (characteristic odor). These reactions can be accounted for by the instability of the bond between the benzoylamino group and the carbon with the double bond.

No changes at all took place in the substance on benzoylation of the acid with benzoyl chloride in pyridine; this furnished further confirmation of the absence from the compound of imino, mercapto and hydroxy groups.

We have previously confirmed the structure of the α-penicillamide of phenylpenicilloic acid [18].

Attempts have previously been made to prepare phenylpenicillin by heating phenylpenicilloic acid; by this method a preparation with very poor antibiotic activity was obtained [19]. It seemed to us that this problem might be solved by starting from 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid and heating it in an inert solvent in order to induce the hydrogen of the ring amino bond to migrate to the double carbon-carbon bond and thereby create a thiazolidine-β-lactam system. The experimental conditions and the absence of agressive substances should favor the continued existence of the β-lactam ring of phenylpenicillin if one had been formed. We failed, however, to convert 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid into phenylpenicillin by heating the free acid or its sodium salt in anhydrous pyridine at 90-95°. The acid was recovered nearly unchanged.

EXPERIMENTAL

4-Chloromethylene-2-phenyl-5-oxazolone (I). 17 g 4-hydroxymethylene-2-phenyl-5-oxazolone, 50 ml anhydrous dichloroethane and 20 g phosphorus pentachloride were heated at 45-50°; the azlactone rapidly went into solution with considerable evolution of hydrogen chloride. After 5 minutes, the reaction mass was transferred to a refrigerator and on the following day the precipitate of 4-chloromethylene-2-phenyl-5-oxazolone was filtered off, washed with a little cold dichloroethane and dried. After removal of the dichloroethane and phosphorus oxychloride from the mother liquor in vacuum, the residue was recrystallized from a small amount of dichloroethane; in this way a further small quantity of azlactone was obtained. The whole of the azlactone was recrystallized from a small amount of dichloroethane containing carbon. After cooling, the solid was filtered, washed with dichloroethane and dried. Yield 9 g with m.p. 126-127°. Readily soluble in ether, methyl alcohol, acetone, ethyl acetate, chloroform, dioxane and benzene; very poorly soluble in cold and more soluble in warm ligroin . Gives an orange-yellow color in pyridine.

α-Benzoylamino-β-chloroacrylamide. 0.5 g 4-chloromethylene-2-phenyl-5-oxazolone was treated in 3 ml methanol with 2 ml of 20% ammonia solution. The azlactone rapidly went into solution. After 3 hours the reaction mass was evaporated to dryness on a water bath in vacuum. The residue was dissolved in a little warm dichloroethane. On cooling, pale-yellow crystals came down and after recrystallization from water they melted at 162-164°. Pale-yellow, stout needles. Readily soluble in methanol, acetone and ethyl acetate, very poorly soluble in ether, chloroform and benzene, insoluble in gasoline.

Found %: N 12.02, 11.86; Cl 15.69. $C_{10}H_9O_2N_2Cl$. Calculated %: N 12.47; Cl 15.81.

α-Benzoylamino-β-chloroacrylic acid (II). 0.5 g 4-chloromethylene-2-phenyl-5-oxazolone was shaken with 5 ml of 1 N solution of sodium hydroxide for 15 minutes. Unreacted azlactone was filtered off. The filtrate was acidified with concentrated hydrochloric acid and α-benzoylamino-β-chloroacrylic acid was precipitated. This was purified by reprecipitation from solution of the sodium salt and dried in a desiccator.

α-Benzoylamino-β-chloroacrylic acid forms white crystals, poorly soluble in water. M.p. 157-158°. Readily soluble in methyl alcohol, acetone, ethyl acetate and dioxane, poorly soluble in ether and chloroform, insoluble in benzene and gasoline.

Found %: Cl 15.88. $C_{10}H_8O_3NCl$. Calculated %: Cl 15.74.

0.5 g α-benzoylamino-β-chloroacrylic acid was dissolved in 7 ml of 1 N sodium hydroxide solution and stood for 48 hours. A small quantity of colorless prisms came down. M.p. 128-129°. No depression of melting point in admixture with benzamide.

Found %: N 11.53, 11.63. C_7H_7ON. Calculated %: N 11.57.

After separation of the benzamide, the filtrate was acidified with concentrated hydrochloric acid but no precipitate was formed. Slow evaporation of the water resulted in separation of small yellowish needles and druses off the same needles which were filtered off and washed with a small amount of water cooled to 0°. Very easily soluble in water, contain chlorine. M.p. 136-137° (with decomp.).

Found %: Cl 9.98. $C_{17}H_{15}O_4N_2Cl$. Calculated %: Cl 10.24.

Judging by the analysis, the substance is the product of addition of benzamide to α-benzoylamino-β-chloroacrylic acid (II).

α-Benzoylamino-β-chloroacrylic acid was oxidized by dissolving 1 g in 10 ml water with addition of a 5% solution of sodium bicarbonate and gradually pouring in 0.1 N potassium permanganate until in a 5-minute test a pink coloration round the brown stain persisted when a sample was placed on filter paper. After 15 minutes, the excess of potassium permanganate was decomposed by addition of a few drops of 30% hydrogen peroxide, and the solution was filtered from manganese dioxide. The weakly alkaline filtrate was evaporated to a volume of 3 ml in vacuum, and the crystals were filtered off and washed with water. M.p. 129-130°. The substance does not exhibit a depression of melting point in admixture with benzamide. Residues of benzamide were isolated from the solution by ether extraction. After removal of the ether, the crystals were identified as benzamide.

After extraction of the benzamide, the aqueous solution was diluted with 10 ml water, acidified with a few drops of acetic acid, heated to the boil and treated with 1 g of calcium chloride in 5 ml water. White crystals came down at once. After boiling for 15 minutes, the hot solution was filtered and the precipitate (0.1727 g) washed with boiling water and dried at 80°.

Found %: CaO 39.54. $CaC_2O_4 \cdot H_{2}O$. Calculated %: CaO 38.4.

In a second oxidation of 1 g α-benzoylamino-β-chloroacrylic acid, 0.39 g benzamide and 0.54 g calcium oxalate were obtained.

Condensation of L-cysteine hydrochloride with α-benzoylamino-β-chloro-acrylamide. 0.14 g L-cysteine hydrochloride and 0.2 g α-benzoylamino-β-chloro-acrylamide were dissolved in 4 ml 1 N sodium hydroxide solution and stood for 48 hours. The mass gave an alkaline reaction and had a yellow color. The nitroprusside reaction for the free mercapto group of cysteine was nearly negative. Acidification of the solution with hydrochloric acid brought down a precipitate which nearly completely dissolved in excess of the acid. The residual tar was separated and the solution treated with active carbon at room temperature. The color changed to pale-pink. The excess of hydrochloric acid was eliminated by careful addition of 10% sodium hydroxide solution until barely acid to congo. White, spherical crystals (druses) began to come down gradually. M.p. 186-187°. The substance does not show a depression of melting point in admixture with the α-amide of desdimethylphenyl-penicilloic acid prepared from L-cysteine hydrochloride and the diethylacetal of formylhippuramide.

Condensation of D, L-penicillamine with 4-chloromethylene-2-phenyl-5-oxazolone. 3 g D, L-penicillamine hydrobromide was dissolved in 26 ml 1 N sodium hydroxide solution, 2.6 g 4-chloromethylene-2-phenyl-5-oxazolone was added, and the whole was stirred for 1 hour. The alkaline reaction to phenolphthalein disappeared. After an interval of half an hour, addition was made of 5 lots of 3 ml each of 1N sodium hydroxide solution. Two hours after the addition of the alkali solution, the reaction remained weakly alkaline. The very small precipitate was filtered off and washed with 5 ml of 1 N sodium hydroxide solution. The filtrate was acidified with hydrochloric acid until weakly acid to congo; the precipitate was filtered, washed with water and dissolved in 250 ml ethyl acetate. The solution was washed with 3 lots of 40 ml each of 5 N hydrochloric acid solution and 100 ml water.

From the ethyl acetate solution, washed with hydrochloric acid and water, the substance was extracted with 5% sodium bicarbonate solution. The aqueous solution was concentrated in vacuum to 50 ml and acidified with hydrochloric acid until weakly acid to congo. The precipitate was filtered off, washed with hot water and recrystallized three times from 30% alcohol. Very fine, pale-yellow polyhedra of 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid were obtained. M.p. 175-177° (with decomp.). Yield 1.65 g (43.2%).

The compound is nearly insoluble in water, dilute mineral acids, ether and benzene; it does not give reactions for chlorine or mercapto or aldehyde groups. It titrates like a monobasic acid.

Found %: C 55.92, 55.99; H 5.05, 5.00; N 8.64; S 10.02. $C_{15}H_{16}O_4N_2S$. Calculated %: C 56.25; H 5.03; N 8.75; S 9.99.

The acidic solution, after separation of the solid, and the wash liquor were combined and neutralized with sodium bicarbonate until weakly acidic to congo. The substance was extracted from the aqueous solution 3 times with 50 ml portions of ethyl acetate, and it was again extracted from this solvent with 5% sodium bicarbonate solution. After blowing air through the solution and acidifying it with hydrochloric acid until weakly acidic to congo, 0.42 g of a crystalline precipitate came down. This was purified by reprecipitation from 20 ml of 1 N hydrochloric acid and dried in a vacuum-desiccator. Colorless crystals with m.p. 180-182° (with decomp.).

The α-penicillamide of phenylpenicilloic acid is poorly soluble in water and gradually comes out in the form of prisms when the solution is evaporated on a water bath in vacuum at 40°. Soluble in alcohol, acetone, ethyl acetate, and dilute mineral acids, insoluble in ether. It is oxidized by iodine solution. It slowly reduces silver and corresponds to the α-penicillamide of phenylpenicilloic acid (VII).

Found %: C 50.62; H 5.38; N 8.57. $C_{20}H_{27}O_6N_3S_2$. Calculated %: C 51.17; H 5.75; N 8.95.

<u>Proof of the structure of 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid.</u> a) 1 g acid was dissolved in 15 ml 85% formic acid, saturated with hydrogen chloride, and refluxed for $2\frac{1}{2}$ hours. The formic acid was distilled off in vacuum. The residue was treated with 10 ml acetone and left in a refrigerator. The precipitate (0.25 g) was filtered off, washed with acetone, and recrystallized by dissolving in a small amount of water with carbon and evaporating down to a volume of 2 ml. Colorless prisms with m.p. 215-216° (decomp.) of the hydrochloride of phenylpenicilloic acid (VIII).

Found %: C 50.81; H 5.82; N 8.54, 8.57. $C_{14}H_{19}O_3N_2SCl$. Calculated %: C 50.84; H 5.79; N 8.46.

It was found to be identical with the substance obtained from penicillamine hydrochloride and formylhippuric acid diethylacetal described in the literature [16].

b) 1 g of the acid was stirred in 10 ml hydrochloric acid at room temperature for 3 days. Dilution of the solution with 50 ml water brought down a small amount of the original substance (0.53 g) which was filtered off, and the solution was dried in a vacuum-desiccator over caustic alkali and sulfuric acid. This substance was dissolved in 4 ml acetic anhydride and 0.5 ml anhydrous pyridine, heated 10 minutes on a boiling water bath and left in a refrigerator. The yellow, crystalline precipitate (0.015 g) was filtered off, washed with acetic anhydride and dried in a vacuum-desiccator. M.p. 174-175° after recrystallization from toluene. The melting point was not lowered after admixture with 4-acetothiomethylene-2-phenyl-5-oxazolone.

c) 1 g of the substance was dissolved in 10 ml water in presence of 1 g sodium bicarbonate and oxidized with a 1 N solution of potassium permanganate as described for the oxidation of α-benzoylamino-β-chloroacrylic acid. The solution was filtered from the precipitate of manganese dioxide and the latter was washed several times with water. The filtrate was evaporated nearly to dryness in vacuum and the crystals of benzamide were filtered off. M.p. 128-129°. Another 0.05 g benzamide was recovered from the mother liquor by extraction with ether.

The aqueous solution, after extraction of the acetamide, was acidified with hydrochloric acid and the resultant very small precipitate was filtered. Oxalic acid was found in the filtrate and isolated as calcium salt in the usual manner.

Found %: CaO 39.40. $CaC_2O_4 \cdot H_2O$. Calculated %: CaO 38.30.

d) Ammonia was liberated on heating 1 g of 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid with 12.5 ml of 1 N solution of sodium hydroxide. After 8 hours, the solution was cooled, acidified with hydrochloric acid and treated with ether. Removal of the ether left 0.32 g colorless crystals with m.p. 120-122°, corresponding to benzoic acid.

e) 0.5 g 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid was dissolved in 5 ml anhydrous pyridine and 0.25 ml benzoyl chloride was added. After a few hours, the pyridine was driven off in vacuum, the residue was dissolved in 5% sodium bicarbonate solution, and the traces of pyridine together with water were removed in vacuum. The dry residue was dissolved in 10 ml water and acidified with hydrochloric acid until weakly acid to congo. The precipitate was filtered, washed with water, dried, and washed with ether. Weight 0.47 g. After recrystallization from 30% alcohol it had m.p. 174-176° (decomp.). It was identical with the compound taken into reaction. Benzoic acid was found in the ethereal solution.

On heating 0.2 g 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid with 3 ml alcohol and 0.5 ml concentrated acid, the characteristic odor of ethyl benzoate was at once developed.

SUMMARY

1. The reaction of 4-chloromethylene-2-phenyl-5-oxazolone with sodium hydroxide solution, ammonia and cysteine was studied.

2. Condensation of the azlactone with penicillamine under caustic alkaline conditions gave 1-thia-3-benzoylamino-4-keto-5-aza-7, 7-dimethyl-2-cycloheptene-6-carboxylic acid and the α-penicillamide of phenylpenicilloic acid.

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THE PROBLEM OF THE MECHANISM OF THE ARBUZOV REARRANGEMENT

IV. REACTION OF α, β-DIBROMOETHYL ALKYL ETHERS WITH TRIISOPROPYL PHOSPHITE

V. S. Abramov and A. I. Bolshakova

It was previously reported [1] that the Arbuzov rearrangement of aliphatic phosphite prepared from primary alcohols and α, β-dibromoethyl alkyl ethers and other active halogenated derivatives proceeds in two separate and independent steps. It was interesting to study the behavior of phosphites obtained from secondary aliphatic alcohols in analogous Arbuzov rearrangements. The results obtained were especially interesting in connection with the fact that the ionic mechanism of the Arbuzov rearrangement proposed by Gerrard and Green [2] and accepted by Pudovik [3] assumes that the product of reaction of a halogenated derivative with a phosphite is the $[(RO)_3PR^{a}]^+$ ion which breaks down by a monomolecular mechanism in a second step. This assumption was not confirmed in any of the experiments.

The substance chosen for investigation was triisopropyl phosphite, and we reacted this with α, β-dibromoethyl methyl, α, β-dibromodiethyl and α, β-dibromoethyl butyl ethers and with methyl α-β-dibromopropionate. The reactions were performed, as previously described, at room temperature. The progress of the reactions was followed from the change in physical properties: refractive index, specific gravity and surface tension. The surface tension was determined by Rebinder's technique [4], based on observation of the maximum pressure of bubbles. The determination was performed in a nitrogen atmosphere with two tips in parallel.

The end of the reaction was assumed to be the instant at which the above-mentioned properties of the reaction mixture underwent no further change. This stage was reached in 3 to 5 days. Results obtained are presented in Table 1, which first gives the values determined immediately after mixing while cooling and then gives the final values.

TABLE 1

Changes of Physical Properties With Time of Reaction Mixtures of Iso-$(C_3H_7O)_3P+CH_2BrCHBrOR$

R	Immediately after mixing			Values established		
	n_D^{20}	d_4^{20}	σ^{20}	n_D^{20}	d_4^{20}	σ^{20}
OCH_3	1.4456	1.2334	23.97	1.4424	1.2622	26.53
OC_2H_5	1.4463	1.2265	24.10	1.4426	1.2498	26.93
OC_4H_9	1.4458	1.1802	25.48	1.4430	1.2017	26.47
$COOCH_3$ . . .	1.4466	1.2303	24.83	1.4292	1.2417	26.27

Mixing of triisopropyl phosphite with α, β-dibromethyl alkyl ethers and with the methyl ester of α, β-dibromopropionic acid is accompanied by appreciable release of heat. Thus, for example, on mixing triisopropyl phosphite with α, β-dibromoethyl methyl ether (cooled to $-10°$), the temperature rose to $+30°$ in 10 minutes; similarly, the temperature rose to $+85°$ in 15 minutes after mixing with the methyl ester of α-β-dibromopropionic acid.

TABLE 2

Molar Refractions and Parachors of the Products

$$\text{Iso-}(C_3H_7O)_3\overset{\displaystyle Br}{P}-\underset{\displaystyle R}{\underset{|}{CH}}-CH_2Br$$

R	MR_D		[P]	
	found	calculated	found	calculated
OCH_3 . . .	89.37	87.29	766.0	763.4
OC_2H_5 . .	93.25	91.90	802.0	802.4
OC_4H_9 . .	103.24	101.15	883.4	880.4
$COOCH_3$.	94.28	91.96	820.5	808.2

TABLE 3

Physical Properties of Isopropyl Esters of α-Alkoxy-β-Bromoethylphosphinic Acids $\text{Iso-}(C_3H_7O)_2\underset{\displaystyle O}{\underset{\|}{P}}-\underset{\displaystyle OR}{\underset{|}{CH}}-CH_2Br$

R	Boiling point	n_D^{20}	d_4^{20}	σ^{20}	MR_D	
					found	calculated
CH_3	128—129° (4 mm)	1.4505	1.2653	30.12	64.45	64.05
C_2H_5	129—131 (4 mm)	1.4476	1.2295	26.67	69.01	68.67
C_4H_9	143—144 (3 mm)	1.4497	1.1809	21.35	78.37	77.90

The tabulated data, the release of heat when the reacting substances are mixed, and the disappearance of the odor of the α, β-dibromoethyl alkyl ethers and of the specific odor of the phosphites indicate the occurrence of a reaction between phosphite and halogenated ethers, probably with formation of an intermediate addition product. The products of this reaction are viscous, colorless liquids.

On the basis of the final values of physical properties, we can calculate the molar refractions and parachors on the assumption of formation of an intermediate product of addition. The observed and calculated values are in satisfactory agreement. The molar refractions found are higher than the calculated values by approximately the same amounts as were observed previously. Results are presented in Table 2.

The product of reaction is probably an intermediate addition product or possibly an equilibrium mixture of a complex and the starting products; products of decomposition are unlikely to enter into the composition of the equilibrium mixture. The reaction product undergoes thermal breakdown in accordance with the second step of the Arbuzov rearrangement. Decomposition commences at a bath temperature of 110-160°. In all cases isopropyl bromide is split off in a yield of 82-87%. The yield of isopropyl bromide in the breakdown of the product of reaction of methyl α, β-dibromopropionate with phosphite was 150%, which is difficult to explain. The residue after thermal breakdown gives isopropyl esters of α-alkoxy-β-bromoethylphosphinic acids. However, the methyl ester of α-isopropoxyphosphono-β-bromopropionic acid was not obtained. Resinification occurs on distillation.

On heating to 120-150°, α,β-dibromoethyl alkyl ethers react violently with phosphite with resinification, and no definite products could be isolated. This confirms the presence of an intermediate addition product.

Data for the isopropyl esters of α-alkoxy-β-bromoethylphosphinic acids are presented in Table 3.

Slight partial decomposition occurs when the esters are fractionated.

The experimental material obtained in the study of the reactions of α-β-dibromoethyl alkyl ethers with triisopropyl phosphite leads to the conclusion that the Arbuzov rearrangement goes in two separate and independent steps, in opposition to the ideas expounded by A. N. Pudovik [3].

Hydrogen bromide was split off from the isopropyl esters of α-alkoxy-β-bromoethylphosphinic acids by treatment with an alcoholic solution of potassium hydroxide. The products were isopropyl esters of α-alkoxyvinylphosphinic acids (Table 4). The product of reaction of methyl α, β-dibromopropionate with isopropyl phosphite, after decomposition at 100-110°, was taken in the reaction leading to release of hydrogen bromide. The methyl ester of α-isopropoxyphosphonoacrylic acid was obtained. The yield of ester from the crude product was small. The phosphorus content was higher than the theoretical, probably due to impurities. Analysis for the double bond by the bromide-bromate method gave 92%.

TABLE 3 (continued)

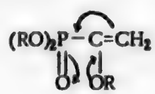
[P] found	[P] calculated	Yield (%)	Bromine content (%) found	Bromine content (%) calculated	Phosphorus content (%) found	Phosphorus content (%) calculated
561.8	562.9	74.9	26.31. 26.32	26.40	9.97. 10.36	10.23
585.9	584.8	75.1	25.22. 25.20	25.23	9.52. 9.63	9.78
628.1	628.6	50.8	23.34. 23.19	23.20	8.91. 8.93	8.98

TABLE 4

Isopropyl Esters of α-Alkoxyvinylphosphinic Acids $\text{Iso-}(C_3H_7O)_2P(=O)-C(R)=CH_2$

R	Boiling point	n_D^{20}	d_4^{20}	σ^{20}	MR_D found	MR_D calc.	[P] found	[P] calc.	Yield (%)	Phosphorus content (%) found	Phosphorus content (%) calc.
OCH_3 .	105—106° (3 mm)	1.4375	1.0657	31.04	54.9	55.8	491.7	493.5	63.4	13.63. 13.55	13.90
OC_2H_5 .	110—112 (4 mm)	1.4340	1.0219	28.11	60.19	60.42	531.9	532.5	76.0	12.92. 12.87	13.13
OC_4H_9 .	128—129 (4 mm)	1.4366	0.9903	27.25	69.79	69.66	609.0	610.5	52.0	11.57. 11.46	11.74
$COOCH_3$	95—97 (11 mm)	1.4060	1.0170	23.71	60.62	60.44	540.1	538.1	25.0	13.83. 14.09	12.35

The prepared esters of α-alkoxyvinylphosphinic acids were examined for their susceptibility to polymerization. Their molecules possibly possess a polar character and they may be represented by the formula



It was found that the esters are not polymerized in presence of peroxides, diazoaminobenzene and zinc chloride. The negative results may be due to steric hindrance or to weakening of the polarity of the double bond by the alkoxy group.

The experimental work was carried out as described previously [1].

SUMMARY

1. Triisopropyl phosphite reacts with α, β-dibromoethyl alkyl ethers and with methyl α, β-dibromopropionate probably in two separate and independent steps with formation of an intermediate addition product in the first step.

2. Thermal breakdown of the addition products leads to formation of isopropyl esters of α-alkoxy-β-bromoethylphosphinic acids (Table 3).

3. Isopropyl esters of α-alkoxyvinylphosphinic acids (Table 4) are formed which do not polymerize with peroxides, diazoaminobenzene and zinc chloride.

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MIXED ESTERS OF DI-TERT-(1,1,1-TRICHLORO)-BUTYLPHOSPHOROUS ACID

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Full esters of phosphorous acid in the chemically pure form were first isolated and described by A. E. Arbuzov in 1905 [1]. Subsequently chemists synthesized a large number of different esters of phosphorous acid [2]. Special interest was attached to the synthesis of mixed esters of phosphorous acid because their transformation into esters of alkylphosphinic acids throws additional light on the mechanism of the Arbuzov rearrangement. The following types of compounds were prepared: fatty-aromatic mixed phosphites [3], various mixed cyclic esters of glycol-phosphorous acids [4], pyrocatechylphosphprous acid [5], and dicyclohexyl-1, 1-diol-phosphorous acids [6]. Work on mixed aliphatic esters of phosphorous acid has recently been reported [7].

Esters of phosphorous acid with tertiary alcohols have not been studied at all (or only to a slight extent). In 1927 Chrzaszcrewska and Sobieranski [8] described the action of phosphorus trichloride on acetone cyanohydrin which gave the corresponding full ester of phosphorous acid. The properties of the latter were unusual for phosphites and were not closely studied. In 1952 Kosolapoff [9] reported that the action of phosphorus trichloride on anhydrous trimethylcarbinol in presence of dimethylaniline in a medium of dry ligroin led to the corresponding phosphite. The latter did not undergo rearrangement. Joung [10] repeated Kosolapoff's experiments and conclusively proved that the product formed under these conditions is di-tert-butylphosphorous acid whose constants were identical with the product obtained by Kosolapoff. The crude product had a slightly high refractive index, but subsequent fractionations invariably gave di-tert-butylphosphorous acid.

Gerrard and Wyvill [11] investigated the influence of structure on the reactivity of tertiary alcohols and found that heating of chloretone with phosphorus trichloride on a water bath gives a mixture of diacid chloride and monoacid chloride. In presence of pyridine the diacid chloride only reacts with one mole of acetone chloroform, while the monoacid chloride does not react at all. Gerrard and co-workers [12] studied the action of phosphorus trichloride on 2, 2, 2-trichloroethanol and 1, 1, 1, 3, 3, 3-hexachloropropanol-2 and showed that the latter compounds react with difficulty or not at all with phosphorus trichloride. In presence of pyridine, however, the reaction goes with facility with formation of the corresponding phosphites and pyridine hydrochloride. This behavior of halogen-substituted alcohols towards halogenated compounds of phosphorus is explained by the lowering of the reactivity of the alcohol due to the influence of the chlorine atoms and the formation of a hydrogen bond with chlorine. Pyridine breaks the hydrogen bond and weakens the influence of the chlorine atoms, thereby rendering the alcohol reactive.

In the present investigation we studied the formation of esters of phosphorous acid from tertiary alcohols. For this purpose we tried to repeat the work of Gerrard* on the synthesis of phosphite from phosphorus trichloride and chloretone in presence of pyridine in a medium of dry ether. Phosphite was not detected, however, in this reaction; monoacid chloride and unchanged chloretone were obtained. Diacid chloride is similarly formed when using a molar ratio of phosphorus trichloride to chloretone. The acid chlorides were used as starting substances for syntheses of mixed esters.

We describe below the syntheses of mixed esters from the monoacid chloride of di-tert-(1, 1, 1-trichloro)-butylphosphorous acid and various alcohols in presence of pyridine in a medium of dry ether. The reaction was

* We did not have access to the paper of W. Gerrard and P. Wyvill in Research (London), 2, 536 (1949). The constants are not given in the abstract [11], and we therefore give a full characterization of all compounds.

TABLE 1

Physical Properties and Analyses of Esters of Phosphorous Acid $\left[\begin{matrix}(CH_3)_2CO \\ | \\ CCl_3\end{matrix}\right]_2 POR$

Preparation no.	R	Boiling point (mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	Yield (%)	Chlorine content (%) found	Chlorine content (%) calc.	Phosphorus content (%) found	Phosphorus content (%) calc.
1	CH_3	152—154° (4 mm). . . .	1.4317	1.5040	85.82	86.03	82.0	51.24	51.27	7.48	7.47
2	C_2H_5	160—160.5 (4 mm) . . .	1.4190	1.5028	89.79	90.64	88.3	49.72. 49.76	49.60	7.04. 7.27	7.22
3	n-C_3H_7	168—169 (3 mm)	1.3853	1.4998	94.13	95.26	90.0	48.06. 48.16	48.03	6.98. 7.08	6.99
4	n-C_4H_9	171.5—172.5 (3 mm). . .	1.3440	1.4997	100.20	99.88	66.5	46.39. 46.55	46.55	6.89. 6.84	6.77
5	n-C_8H_{17}	202—203 (4 mm). . . .	1.2546	1.4890	118.01	118.35	71.0	41.16. 41.30	41.47	6.14. 6.25	6.04
6	iso -C_4H_9	166—167 (2.5 mm) . . .	1.3397	1.4960	99.88	99.88	53.5	46.50. 46.56	46.55	6.95. 6.95	6.77
7	—CH_2 . . .	60—61° (M.p.)	—	—	—	—	68.0	44.30. 44.00	44.23	6.34. 6.36	6.44
8	iso- C_3H_7	166 (4 mm).	1.3808	1.4986	94.13	95.26	74.5	48.11. 47.97	48.03	6.85. 6.76	6.99
9	sec -C_4H_9 . . .	171—173 (4 mm). . . .	1.3596	1.5010	99.04	99.88	76.6	46.97. 47.01	46.55	6.40. 6.48	6.77
10	C_6H_{11}	198 * (4 mm).	1.3721	1.5082	105.00	105.19	74.5	44.00. 43.90	44.04	6.40. 6.39	6.41
11	C_6H_5	208 (4 mm).	1.4101	1.5405	106.12	105.52	63.0	44.46. 44.51	44.60	6.48 .6.69	6.49

* Crystallized after distillation; m.p. 46-47°.

carried out at a temperature of 0-5° with subsequent heating to the boiling point of ether. Primary alcohols of normal and secondary structures as well as secondary, cyclic and tertiary alcohols were taken into reaction. Normal primary alcohols (methyl, ethyl, propyl, butyl and octyl) react in the cold with the acid chloride with formation of the corresponding mixed ester and with precipitation of pyridine hydrochloride. Yields of esters were high (70 to 90%). The esters are viscous, colorless liquids; their constants and analyses are presented in Table 1 (nos. 1-5).

Primary alcohols (isobutyl and furyl), and secondary alcohols (isopropyl, sec-butyl) and cyclohexyl alcohol also react with facility under cooling with the monoacid chloride of di-tert-(1, 1, 1-trichloro)-butylphosphorous acid in presence of pyridine and give the corresponding mixed esters in good yields. Their physical characteristics are set forth in Table 1 (nos. 6-10). The furyl ester was crystalline. After two recrystallizations from ligroin it has m.p. 60-61°. It decomposes when distilled in vacuum. The cyclohexyl ester of di-tert-(1, 1, 1-trichloro)-butylphosphorous acid was distilled in vacuum and characterized; it crystallized when kept; m.p. 46-47°.

Phenol gives an extremely stable mixed ester with the monochloride; it distills in vacuum almost without decomposition at high temperature.

The reactions of di-tert-(1, 1, 1-trichloro)-butylphosphorous acid monochloride with tertiary alcohols are of particular interest. The reactions were carried out with trimethylcarbinol, acetone cyanohydrin and chloretone in presence of pyridine in a medium of dry ether, at the start with cooling and later with heating to the boiling point of ether. The corresponding phosphites were not obtained although tertiary alcohols with various degrees of reactivity were taken. Trimethylcarbinol contains a normally reactive hydroxyl group, but neither we nor Joung [9, 10] obtained phosphites with it. Acetone cyanohydrin gives a phosphite [8] with phosphorus trichloride and does not give a mixed ester. The reactivity of chloretone is inhibited but it reacts in presence of pyridine. However, it likewise does not give a phosphite. A mixture of mono- and diacid chlorides was isolated from the reaction products.

TABLE 2

Complex Compounds of Mixed Phosphites With Cuprous Chloride

$$\left[\begin{array}{l}(CH_3)_2CO \\ \quad\;\;\; | \\ \quad\;\; CCl_3\end{array}\right]_2 POR \cdot CuCl$$

R	Melting point	Chlorine content (%) found	Chlorine content (%) calc.	Phosphorus content (%) found	Phosphorus content (%) calc.
CH_3	182—183°	47.96	48.25	5.95	6.02
C_2H_5	178 (with decomp.)	46.93. 46.72	47.01	5.97. 5.83	5.87
n-C_3H_7	138 (with decomp.)	45.45	45.80	5.93	5.72
n-C_4H_9	162 (with decomp.)	44.73. 44.88	44.64	5.69. 5.70	5.57
n-C_8H_{17}	Obtained in the form of syrup				
iso-C_4H_9	191 (with decomp.	44.50. 44.56	44.64	5.48. 5.50	5.57
—CH_2	136 (with decomp.	42.81. 42.78	42.80	5.43. 5.42	5.34
iso-C_3H_7	184 (with decomp.)	45.61. 45.52	45.80	5.50. 5.51	5.72
sec-C_4H_9	172 (with decomp.)	44.41. 44.43	44.64	5.44. 5.41	5.57
C_6H_{11}	182 (with decomp.)	42.40. 42.45	42.63	5.28. 5.28	5.32
C_6H_5	156	42.90. 42.81	43.09	5.30. 5.25	5.38

The monoacid chloride of di-tert-(1, 1, 1-trichloro)-butylphosphorous acid reacts with ordinary alcohols (methyl and ethyl) in the absence of pyridine with formation of acid. Considerable heat is developed when the reaction is carried out in presence of water. In these reactions the monoacid chloride behaves like the others although its reactivity is slightly reduced. We prepared di-tert-(1, 1, 1-trichloro)-butylphosphorous acid by the

action of an equimolar amount of water on the acid chloride, and we characterized the acid [13]. Both the reactivity and steric hindrance influence the formation of phosphites with tertiary alcohols. In these reactions we consider that a predominating and possibly a decisive part is played by steric hindrance.

As true derivatives of trivalent phosphorus, all the mixed esters that were prepared react with monohalides of copper. The esters react energetically with cuprous chloride. Well-crystallized complexes are formed except with the n-octyl ester which gives a viscous, honey-like, non-crystallizing product. The properties and analyses of the complex compounds of the mixed esters with cuprous chloride are presented in Table 2.

EXPERIMENTAL

Preparation of the diacid chloride of tert-(1, 1, 1-trichloro)-butylphosphorous acid. 137.5 g phosphorus and 177.5 g anhydrous chloretone in 500 ml dry ether were placed in a one-liter round-bottomed flask fitted with thermometer, dropping funnel, mechanical stirrer and reflux condenser closed with a calcium chloride tube. The flask was cooled with ice and salt until the temperature of the reaction mixture fell to 0°. 79 g dry pyridine was then introduced with vigorous stirring at such a rate that the temperature did not rise. After the pyridine had been run in, the mixture was stirred at room temperature for 1 hour and heated to the boiling point of ether. The pyridine hydrochloride was quickly filtered off, the ether was driven off, and the residue was fractionated in vacuum. Two consecutive distillations gave a fraction with b.p. 118° (16 mm): a readily mobile liquid which fumed in the air. Yield 201 g (75.5%).

n_D^{20} 1.5236, d_4^{20} 1.5280, MR_D 55.53; calculated 55.58

Found %: Cl 63.40, 63.48; P 11.00, 11.06. $C_4H_6OPCl_5$. Calculated %: Cl 63.60; P 11.17.

Preparation of the monochloride of di-tert-(1, 1, 1-trichloro)-butylphosphorous acid. 355 g chloretone and 158.2 g pyridine in 200 ml dry ether were placed in a one liter three-necked flask fitted with thermometer, dropping funnel, mechanical stirrer and reflux condenser closed with a calcium chloride tube. To the cooled and stirred mixture was added 137.6 g phosphorus trichloride at such a rate that the temperature did not rise above 0°. Stirring was thereafter continued for 1 hour at room temperature and for ½ hour with heating to the boiling point of ether. The pyridine hydrochloride was rapidly filtered off, the ether was driven off, and the residue distilled in vacuum. Three successive fractionations gave a fraction with b.p. 171° at 5 mm. Yield 330 g (78.5%).

n_D^{20} 1.5265, d_4^{20} 1.5192, MR_D 84.50; calculated 84.64.

Found %: Cl 59.06, 58.92; P 7.25, 7.26. $C_8H_{12}O_2PCl_7$. Calculated %: Cl 59.18; P 7.39.

Preparation of 1, 1, 1-trichloro-tert-butyl ester of phosphorous acid. 185.0 g chloretone and 82.5 g pyridine in 200 ml dry ether were placed in a one liter three-necked flask. To the mixture was added 49.6 g phosphorus trichloride at such a rate that the temperature did not rise above 0°. The mixture was thereupon stirred at room temperature and with heating to the boiling point of ether for 1½ hours. The pyridine hydrochloride was rapidly filtered off, the ether was driven off, and the residue was fractionated in vacuum. Fractionation proceeded with difficulty. Several fractionations gave pyridine (19 g), chloretone (53 g) and a fraction with b.p. 170-171° (5 mm) and the constants n_D^{20} 1.5257, d_4^{20} 1.5187, corresponding to the monochloride of tert-(1, 1, 1-trichloro)-butylphosphorous acid. Yield 101 g (66.5%).

Preparation of mixed esters of di-tert-(1, 1, 1-trichloro)-butylphosphorous acid. 0.1 mole alcohol and 0.1 mole pyridine in 200-300 ml dry ether were placed in a half-liter three-necked flask fitted with thermometer, dropping funnel, mechanical stirrer and reflux condenser closed with a calcium chloride tube. To the mixture (cooled with ice and salt) was added 0.1 mole of the monochloride of di-tert-(1, 1, 1-trichloro)-butylphosphorous acid diluted with a small quantity of ether; the rate of addition was such that the temperature of the reaction mixture did not rise above 0°. After the monochloride had been added, stirring was continued at first at room temperature and later with heating to the boiling point of ether for 1½ to 2 hours. The pyridine hydrochloride was rapidly filtered off, the ether was distilled off, and the residue was distilled in vacuum. After two to three successive fractionations the pure mixed ester was usually obtained. The constants and analyses of the mixed esters are given in Table 1.

Preparation of complex compounds of mixed esters with cuprous chloride. To 4-5 g phosphite in a test tube was added the calculated amount of cuprous chloride in one portion. The mixture was stirred with a thermometer and the rise of temperature was measured. The mixture was then carefully heated (120-160°) until nearly the

whole of the cuprous chloride had dissolved. Cooling then resulted in solidification to a dense mass. The product was dissolved in a 1 : 1 mixture of anhydrous alcohol and gasoline (b.p. 70-120°) and filtered through a glass filter. The crystals were collected and recrystallized once or twice. Beautifully formed crystalline complexes were obtained with all the esters (except that of n-octyl alcohol) and the majority melted with decomposition. Data for the complexes are presented in Table 2.

SUMMARY

1. Steric factors play an important, if not decisive, role during formation of esters of phosphorous acid with tertiary alcohols.

2. Mixed esters of di-tert-(1, 1, 1-trichloro)-butylphosphorous acid with primary and secondary alcohols and phenol were obtained. Phosphites were not formed with tertiary alcohols.

3. Mixed esters of di-tert-(1, 1, 1-trichloro)-butylphosphorous acid form complex compounds with cuprous chloride.

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* In Russian.

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N-ACYLAMIDOPHOSPHORIC ACIDS

A. V. Kirsanov and R. G. Makitra

Only one N-acylamidophosphoric acid of the type of $RCONHPO(OH)_2$ has been known up to the present time; this is N-benzoylamidophosphoric acid which was obtained by the action of water on the reaction mixture formed from phosphorus pentachloride and benzamide [1].

It was recently found that treatment of unsubstituted acid amides with phosphorus pentachloride leads to nearly quantitative yields of trichlorophosphazoacyls [2]; when these are treated with formic acid they behave similarly to trichlorophosphazosulfone compounds [3] in forming dichlorides of acylamidophosphoric acids [4]. The reaction with formic acid could not be used for the preparation of the monochlorides and the free acylamidophosphoric acids. Unlike the dichlorides of arylsulfonamidophosphoric acids, which react with formic acid to give satisfactory yields in succession of the monochlorides and the free arylsulfonamidophosphoric acids [3], the dichlorides of acylamidophosphoric acids either do not enter into reaction with formic acid or react at higher temperatures with formation of benzonitrile, phosphorus oxychloride and metaphosphoric acid. This is probably the consequence of the formic acid entering into reaction with the dichlorides of acylamidophosphoric acids at temperatures higher than the temperature of thermal scission of the monochlorides and the free acylamidophosphoric acids.

Hydrolysis of the dichlorides of acylamidophosphoric acids with water in acetone solution did not give the monochlorides of acylamidophosphoric acids, but the free acylamidophosphoric acids were obtained in substantially quantitative yields.

N-Acylamidophosphoric acids are crystalline substances, readily soluble in water and alcohol, insoluble in acetone, ether, benzene and the majority of other organic solvents. All the acylamidophosphoric acids decompose on heating to the melting point, and in some cases the decomposition is accompanied by marked darkening and the evolution of gases (see table). The acylamidophosphoric acids likewise break down when heated in solution, so that they cannot be recrystallized. However, recrystallization is unnecessary since hydrolysis of the pure dichlorides gives perfectly pure acylamidophosphoric acids.

N-Acylamidophosphoric acids are strong acids which displace carbonic and acetic acids from their salts. With methyl orange they titrate as monobasic acids, but with phenolphthalein as dibasic acids. The alkali salts of acylamidophosphoric acids are crystalline; they are soluble in water and more resistant to hydrolysis than the free acids. The melting point, external appearance and analytical data of acylamidophosphoric acids are given in the table.

EXPERIMENTAL

Preparation of acylamidophosphoric acids. 0.055 mole water (1 ml) was added to a solution of 0.01 mole of the dichloride of the acylamidophosphoric acid in 15 ml acetone, and the solution was left in an open dish overnight. With progress of the reaction and with evaporation of the acetone, the free acylamidophosphoric acid came down gradually in the form of well-developed crystals. Development of heat and evolution of hydrogen chloride were observed on addition of the water when the reaction was carried out with large amounts. The following day the dish containing the crystals was placed in a desiccator over potassium hydroxide for several hours, after which the product was mixed with 10 ml hot acetone, filtered at the pump, washed with warm acetone, and dried in a desiccator over potassium hydroxide and sulfuric acid. Yield nearly quantitative.

Acylamidophosphoric Acids of the Type of $RCONHPO(OH)_2$ Prepared According to the Equation: $RCONHPOCl_2 + 2H_2O \rightarrow 2HCl + RCONHPO(OH)_2$

Acyl	Outward appearance	Melting point (with decomposition)	Found				Empirical formula	Calculated	
			% N	% P	equiv. to methyl orange	equiv. to phenolphthalein		% N	% P
Benzoyl	Colorless, fine needles	136—138 *	6.75, 6.89	15.67	0.980, 0.992	1.996, 2.006	$C_7H_8O_4NP$	6.96	15.43
o-Nitrobenzoyl	Light yellow needles	148—149 ***	11.32	12.53	0.975	1.966	$C_7H_7O_6N_2P$	11.39	12.30
p-Nitrobenzoyl	Light yellow needles	178—180 ***	11.40	12.64	0.984	2.011	$C_7H_7O_6N_2P$	11.39	12.30
m-Nitrobenzoyl	Colorless needles	135—137 ***	11.33	12.48	0.953	1.995	$C_7H_7O_6N_2P$	11.39	12.30
2-Chloro-4-nitrobenzoyl	Light yellow needles	135—137	9.85	—	0.997	1.990	$C_7H_6O_6N_2ClP$	9.98	—
3,5-Dinitrobenzoyl	Light yellow needles	149—151 ***	14.35	10.74	0.990	1.995	$C_7H_6O_8N_3P$	14.43	10.64
2,4-Dinitrobenzoyl	Nearly colorless needles	153—155 ***	14.36	10.86	0.944	1.967	$C_7H_6O_8N_3P$	14.43	14.43
o-Chlorobenzoyl	Colorless, fine needles	134—136	5.92	13.06	0.981	1.985	$C_7H_7O_4NClP$	5.94	13.14
m-Chlorobenzoyl	Colorless needles	128—129 **	5.95	13.17	0.965	1.961	$C_7H_7O_4NClP$	5.94	13.14
2,4-Dichlorobenzoyl	Colorless needles	140—142 ***	5.07	11.73	1.032	2.030	$C_7H_6O_4NCl_2P$	5.18	11.48

* According to Titherley and Worrall [1], benzoylamidophosphoric acid melts at 157-158°, which is wrong.

** The substance melts at 128-129° but immediately solidifies and melts again at 188-189°.

*** Decomposition is accompanied by marked darkening and evolution of gases.

**** The methyl orange equivalent for all the compounds is 1; the phenolphthalein equivalent is 2.

SUMMARY

Ten acylamidophosphoric acids were prepared by hydrolysis of the dichlorides of acylamidophosphoric acids.

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INVESTIGATIONS IN THE ISOXAZOLE SERIES

III. SYNTHESIS OF ARYLISOXAZOLES

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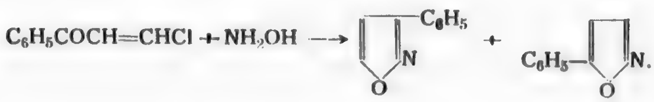
As reported previously [1], one of the most convenient methods of synthesis of alkylisoxazoles is based on the reaction of alkyl-β-chlorovinyl ketones with hydroxylamine. Recently we developed a direct method of synthesis of aryl-β-chlorovinyl ketones [2] which made the latter just as accessible as their aliphatic analogs. Since the arylisoxazoles have been very inadequately studied due to their difficult accessibility, we decided to fill this gap and to develop their synthesis on the basis of aryl-β-chlorovinyl ketones.

It was found that aryl-β-chlorovinyl ketones react with hydroxylamine hydrochloride under the same conditions as their aliphatic analogs [1], i.e. on heating of both components in methanol, with formation of the arylisoxazoles in high yields. As we know [1], reaction of alkyl-β-chlorovinyl ketones with hydroxylamine gives a mixture of α- and γ-isomers (5- and 3-substituted isoxazoles), which contains 50-60% of the α-form. We studied this reaction with phenyl-β-chlorovinyl ketone and established that a mixture of approximately equal parts of α- and γ-phenylisoxazoles is formed in this case:

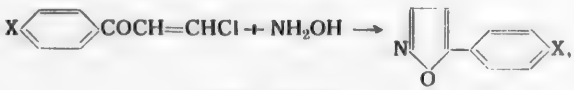


Claisen's method was used for determination of the content of α-isomer in the mixture. This method [3] is based on cleavage of the α-isomer of the isoxazole under the action of sodium alkoxide, with formation of β-ketonitrile. We slightly modified the original method of Claisen and isolated the product of cleavage not in the form of the sodium salt of the ketonitrile but in the form of cyanoacetophenone itself; the completeness of cleavage could be checked in this manner. In spite of this improvement, however, the method of determination of the percentage content of α-isomer cannot be considered analytically accurate; it gives consistently low results. The numerical data obtained by this method, including the data in the present work, therefore bear an indicative character.

Our analysis of the specimen of phenylisoxazole that we prepared showed that more than 62-67% of the α-isomer was present. Complete separation of the two arylisoxazoles met with serious difficulties and we were compelled to abandon the attempt.

Phenyl-β-chlorovinyl ketones substituted in the aromatic nucleus (p-tolyl, p-chloro-, p-nitrophenyl) likewise generally react smoothly with hydroxylamine, with formation of arylisoxazoles in high yields (70-90%). Negative results were obtained only with o-bromophenyl-β-chlorovinyl ketone; the arylisoxazole did not separate when the ketone was reacted with hydroxylamine. In contrast to phenylisoxazole, the arylisoxazoles containing a substituent in the aromatic nucleus were solids. This enabled in the present case a more precise solution of the problem of formation of the isomers. The compounds separated from the reaction mixture in very high yield (up to 90%) had very sharp melting points even before purification and these scarcely changed after

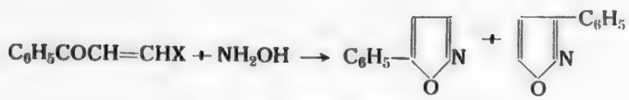
recrystallization. This fact indicates that the prepared compounds are pure substances; nor could a second isomer be isolated from the recrystallization mother liquors. Consequently the reaction of ring-substituted aryl-β-chlorovinyl ketones with hydroxylamine goes only in one direction. We cannot definitely rule out the possibility of formation of very minute amouts of a second isomer, but this possibility cannot in any way detract from the preparative value of the method. The melting point of the prepared p-tolylisoxazole was identical with that of the compound described by Mumm [4] as α-(p-tolyl)-isoxazole, whose structure follows from its transformations. Later on in this paper we submit supporting evidence that the p-nitrophenylisoxazole obtained from p-nitrophenyl-β-chlorovinyl ketone is likewise the α-isomer. It can scarcely be doubted that the p-chlorophenylisoxazole synthesized by the same method is the α-isomer. Consequently the reaction of aryl-β-chlorovinyl ketones, containing substituents in the aromatic ring, with hydroxylamine differs from the analogous reaction with alkyl-β-chlorovinyl ketones in going in only one direction and leading to 5-arylisoxazoles. It is probably the most convenient synthesis of these compounds:



$X = CH_3$, Cl, NO_2.

The new data widen the possibility of synthesis of isoxazole derivatives on the basis of β-chlorovinyl ketones [1] and indicate that the method is a sufficiently general one.

One of us has shown [5] that alkyl-β-dialkylaminovinyl ketones likewise react with hydroxylamine to give excellent yields of alkylisoxazoles, and in this case the reaction goes almost exclusively in the direction of formation of the α-isomer. We can now submit new results for the influence of a substituent in the β-position of a vinyl ketone of the type of RCOCH=CHX as exemplified by phenylisoxazole.

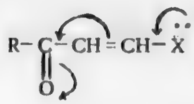


$X = OC_6H_5$, $N(CH_3)_2$, $N(C_2H_5)_2$.

It was found that, just as in the aliphatic series, phenyl-β-dialkylaminovinyl ketones give a high yield of phenylisoxazole consisting of α-isomer to the extent of not less than 90%. The product is very probably substantially pure α-phenylisoxazole since it sets completely to a crystalline mass with m.p. 25-27°. This route is evidently the most convenient for preparation of this compound.

The reaction of phenyl-β-phenoxyvinyl ketone with hydroxylamine gave a 40% yield of phenylisoxazole consisting of α-isomer to the extent of 52%. This result is in agreement with the observation [6] that methyl-β-phenoxyvinyl ketone reacts with hydroxylamine to give a 31% yield of methylisoxazole with an α-isomer content of over 30%. We attempted to prepare an isoxazole by condensing hydroxylamine with a quaternary salt of β-aminovinyl ketone: a salt of β-benzoylvinyltriethyl ammonium; in this experiment, however, phenylisoxazole was obtained in low yield and not perfectly pure; this was probably the consequence of side reactions (possibly hydrolytic fission of the quaternary salt, etc.); this reaction is therefore lacking in preparative interest.

The above results show fairly conclusively that the ratio of the α- and γ-isomers of phenylisoxazole formed is governed by the character of the β-substituent X in the substituted vinyl ketone RCOCH=CHX. In line with the earlier hypothesis of one of us [5], the amount of α-isomer formed increases with the suppression of the electrophilic activity of the carbonyl group in the system:



The ratio of isomeric α- and γ-phenylisoxazoles obtained in their synthesis from dialkylaminovinyl ketone ($X = NR'_2$), phenoxyvinyl ketone ($X = OC_6H_5$) and chlorovinyl ketone ($X = Cl$) indicates that suppression of the electrophilic activity of the carbonyl group is intensified in the order phenoxyvinyl ketone < chlorovinyl ketone < dialkylaminovinyl ketone.

The results obtained in this part of the work compel us to entertain serious doubts about the data of Italian authors [7] who claimed that pure γ-substituted isoxazoles can be obtained by the reaction of alkoxyvinyl ketones with hydroxylamine.

With the objective of confirming our claim that α-(p-nitrophenyl)-isoxazole is actually formed in the reaction of p-nitrophenyl-β-chlorovinyl ketone with hydroxylamine, we carried out experiments on the nitration of a specimen of phenylisoxazole obtained from dialkylaminovinyl ketone and consisting of substantially pure α-isomer. Nitration with a mixture of nitric and sulfuric acids gave a total yield of 68% of a mixture of nitro derivatives which contained over 25% of a substance identical (mixed melting test) with the substance obtained from p-nitrophenyl-β-chlorovinyl ketone. The position of the nitro group in this compound was confirmed by oxidation with permanganate which led to p-nitrobenzoic acid. Notwithstanding that the nitration of phenylisoxazole is a complex process and gives a mixture of nitro derivatives (we are now making a closer study of the problem), the data afford adequate confirmation that p-nitrophenyl-β-chlorovinyl ketone and hydroxylamine actually gave an α-substituted isoxazole.

It is necessary to add that p-nitrophenylisoxazole obtained by us by the above two routes was very similar to the substance described by Musante as γ-(p-nitrophenyl)-isoxazole. The Italian authors, however, nitrated a specimen of phenylisoxazole of unclarified structure, so that the structure of the product of nitration given by the author is not proven. Scrutiny of the paper [8] leads us to the conclusion that Musante actually prepared a compound identical with ours, i.e. α-(p-nitrophenyl)-isoxazole.

EXPERIMENTAL

Arylisoxazoles from β-chlorovinyl ketones. Phenylisoxazole. 63 g phenyl-β-chlorovinyl ketone and 27 g hydroxylamine hydrochloride in 150 ml dry methanol were heated on a water bath for 6 hours. The reaction mixture was cooled and poured into water. The resultant oil was collected and the aqueous layer extracted once with benzene and three times with ether. The combined extracts were dried over magnesium sulfate, the solvent was distilled off, and the residue was distilled in vacuum. The fraction with b.p. 91-93° (3 mm) was phenylisoxazole; yield 38.5-44 g (70-80%), n_D^{20} 1.5826.

Found %: N 9.81, 9.88. C_9H_7ON. Calculated %: N 9.65

Phenyisoxazole is a colorless liquid with a characteristic odor. Literature data for γ-phenylisoxazole: b.p. 156-158° at 28 mm [9]. A solution of 8 g of the prepared phenylisoxazole in 25 ml anhydrous alcohol was added dropwise to a solution of 1 g sodium in 50 ml anhydrous alcohol. The mixture was heated on a water bath for 30 minutes, cooled, and run into water. The resultant homogeneous solution was extracted three times with ether. The ethereal extracts were combined and dried over magnesium sulfate and the ether was driven off. The residue contained a blob of oil; this proved that fission of the sample of phenylisoxazole had been complete. The aqueous layer was acidified with 10% hydrochloric acid until acid to congo and allowed to stand overnight. The next day the precipitate was filtered off and dried in a vacuum desiccator over phosphorus pentoxide. Yield of ω-cyanoacetophenone 5-5.4 g, corresponding to an α-isomer content of 60-67%, m.p. 80-80°. Literature data for ω-cyanoacetophenone 80-81° [10].

α-(p-Tolyl)-isoxazole was prepared similarly from 8 g p-tolyl-β-chlorovinyl ketone and 4 g hydroxylamine hydrochloride in 50 ml dry methanol. Yield 6.5 g (90%), m.p. 52-56°. Recrystallization from ligroin gave white, lustrous crystals with m.p. 58-60°. The literature [4] reports m.p. 60° for α-(p-tolyl)-isoxazole.

Found %: N 8.99, 8.63. $C_{10}H_9ON$. Calculated %: N 8.73.

α-(p-Chlorophenyl)-isoxazole was similarly prepared from 6.1 g p-chlorophenyl-β-chlorovinyl ketone and 2.8 g hydroxylamine hydrochloride in 50 ml dry methanol. Yield 5 g (90%), m.p. 76-79°. Recrystallization from ligroin gave yellow crystals with m.p. 82-82.5°.

Found %: N 7.64, 7.73. C_9H_6ONCl: Calculated %: N 7.79.

α-(p-Nitrophenyl)-isoxazole. 5.6 g p-nitrophenyl-β-chlorovinyl ketone was added to a solution of 2.5 g hydroxylamine hydrochloride in 30 ml methanol and heated on a water bath. After 2 hours the reaction mass turned yellow and a flocculent precipitate came down. Another 30 ml methanol was added and heating continued. After 1½-2 hours the precipitate dissolved. 9 hours after the start of heating, the reaction mixture was cooled and left overnight. The next day the precipitate was filtered. Yield of α-(p-nitrophenyl)-isoxazole 3.5 g (70%), m.p. 165-169°. Recrystallization from glacial acetic acid gave golden-yellow crystals with m.p. 172-174°.

Found %: N 14.51, 14.85. $C_9H_6O_3N_2$. Calculated %: N 14.73.

Nitration of phenylisoxazole. 13.8 g phenylisoxazole, prepared from phenyl-β-dimethylaminovinyl ketone was added dropwise (with vigorous stirring and cooling to −10 to −5°) to 46 ml sulfuric acid (d 1.83). Addition was then made to the mixture (with cooling to −5 to −2°) of a mixture of 21.5 ml nitric acid (d 1.54) and 31 ml sulfuric acid (d 1.83), after which the reaction mass was stirred at room temperature for 30 minutes and poured on to ice. The white crystals were filtered off and dried in a vacuum-desiccator over phosphorus pentoxide. Yield 12.3 g (68%) with m.p. 116-125°. Recrystallization from methanol gave 3.05 g (yield 17% on the phenylisoxazole and 25% on the total amount of products) of colorless crystals with m.p. 171-172°.

Found %: 14.75, 14.86. $C_9H_6O_3N_2$. Calculated %: N 14.73.

A mixed melting test with a specimen obtained from p-nitrophenyl-β-chlorovinyl ketone did not give a depression.

The nitrophenylisoxazole with m.p. 171-172° was boiled with aqueous potassium permanganate to form p-nitrobenzoic acid with m.p. 233°. Recrystallization from water gave lustrous crystals with m.p. 237-237.5°. A mixed melting test with p-nitrobenzoic acid did not give a depression. The literature [11] reports m.p. 238° for p-nitrobenzoic acid.

Reaction of phenyl-β-dialkylaminovinyl ketones with hydroxylamine hydrochloride. 50 g phenyl-β-dimethylaminovinyl ketone and 20 g hydroxylamine hydrochloride in 150 ml dry methanol were heated for 6 hours. The mixture was run into water; after working up by the above method, 29-31.5 g phenylisoxazole (70-76%) was obtained; b.p. 96° at 2 mm, n_D^{18} 1.5840, m.p. 25-27°. 10.5 g of the product was treated with a solution of 2.3 g sodium in 50 ml anhydrous alcohol by the method described above. 9.45-9.55 g of ω-cyanoacetophenone was thus obtained, corresponding to an α-isomer content of 90-91%; m.p. 80-81°. By the above-described procedure, 30 g phenyl-β-diethylaminovinyl ketone and 12.5 g hydroxylamine hydrochloride gave 15.4 g (72%) of phenylisoxazole with b.p. 95-96° at 2 mm, n_D^{20} 1.5844.

Cleavage of the alcoholate as described above shows that the specimen contains 90% of α-isomer.

Reaction of phenyl-β-phenoxyvinyl ketone with hydroxylamine hydrochloride. 10.5 g phenyl-β-phenoxyvinyl ketone [12] and 4.5 g hydroxylamine hydrochloride in 30 ml dry methanol were heated on a water bath for 7 hours. Working-up in the above manner gave phenylisoxazole with b.p. 96° at 2 mm; yield 3 g (39%), n_D^{20} 1.5831.

Treatment of the prepared substance with alcoholate showed that it contained 52% of α-isomer.

Reaction of β-benzoyl-vinyltriethylammonium chloride with hydroxylamine hydrochloride. 22 g of β-benzoyl vinyltriethylammonium chloride [13] and 10 g hydroxylamine hydrochloride in 75 ml dry methanol were heated on a water bath for 10 hours. After working up in the manner described above for phenyl-β-chlorovinyl ketone, phenylisoxazole with b.p. 84° at 1 mm was obtained; yield 2 g (17%), n_D^{20} 1.5830.

SUMMARY

1. Reaction of aryl-β-chlorovinyl ketones with hydroxylamine yields arylisoxazoles; the reaction goes in one direction when the aromatic nucleus contains a substituent, and only α-substituted isomers are obtained.

This reaction can serve as a convenient method of synthesis of arylisoxazoles.

2. The ratio of α- and γ-substituted isoxazoles formed in the reaction of β-substituted vinyl ketones RCOCH=CHX with hydroxylamine is shown to depend on the character of the substituent. Substantially pure α-substituted isomer is formed when $X = NR_2$.

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DERIVATIVES OF HEXAMETHYLENEIMINE

I. SYNTHESIS OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEIMINE

G. S. Kolesnikov and N. N. Mikhailovskaya

Very little study has been devoted to the chemical properties of hexamethyleneimine and its derivatives. Mention is made in the literature of the preparation of N-methylhexamethyleneimine by the action of formaldehyde and formic acid on hexamethyleneimine at 110-115° in sealed vessels [1]; N-methylhexamethyleneimine can also be obtained by reduction of N-methyl-ε-caprolactam with lithium aluminum hydride [2]. N-o-Chlorobenzylhexamethyleneimine has been proposed as an insecticide, but details of its preparation and its properties are not given [3]. Descriptions have been given of the synthesis and properties of such N-ω-hydroxyalkyl derivatives of hexamethyleneimine as N-γ-hydroxypropylhexamethyleneimine, N-β-hydroxypropylhexamethyleneimine, N-β-hydroxyisopropylhexamethyleneimine; these N-derivatives of hexamethyleneimine were obtained by the action of the corresponding hydroxybromo derivatives on hexamethyleneimine [4].

The synthesis of N-alkyl derivatives of hexamethyleneimine was realized by reaction of hexamethyleneimine with alkyl chlorides or bromides, and it was established that alkyl bromides react with hexamethyleneimine with greater facility than alkyl chlorides. At the same time the hydrohalide of hexamethyleneimine is formed, and performance of the reaction necessitates taking not less than 2 moles of hexamethyleneimine for each mole of alkyl halide:

$$2(CH_2)_6NH + RX \rightarrow (CH_2)_6NR + (CH_2)_6NH \cdot HX.$$

An intermediate product of the reaction is evidently the hydrohalide of the N-alkylhexamethyleneimine, reaction of which with unalkylated hexamethyleneimine leads to formation of free N-alkylhexamethyleneimine and the hydrohalide of hexamethyleneimine:

$$(CH_2)_6NH + RX \rightarrow (CH_2)_6NR \cdot HX,$$
$$(CH_2)_6NR \cdot HX + (CH_2)_6NH \rightarrow (CH_2)_6NR + (CH_2)_6NH \cdot HX.$$

We found that increase in the hexamethyleneimine/n-butyl bromide molar ratio from 1 : 1 to 2 : 1 leads to rise in the yield of N-n-butylhexamethyleneimine from 39 to 75%, calculated on the n-butyl bromide. In our opinion this fact confirms the proposed reaction scheme.

The N-alkylhexamethyleneimines that we synthesized and their properties are presented in Table 1.

All the N-alkylhexamethyleneimines are very hygroscopic liquids with a pungent odor and they have well-marked basic properties. This last characteristic permitted determination of the molecular weight of the N-alkylhexamethyleneimines by direct titration with 0.1 N HCl.

We also attempted to prepare N-vinylhexamethyleneimine by the action of vinyl bromide on hexamethyleneimine. No reaction, however, occurred at room temperature and the formation of hexamethyleneimine hydrobromide was not observed; the starting substances were recovered unchanged on distillation of the reaction mixture. An attempt to synthesize N-vinylhexamethyleneimine by splitting off water from N-β-hydroxyethylhexamethyleneimine by distillation over solid caustic potash was likewise unsuccessful. N-Vinylhexamethyleneimine could not be prepared by vinylation of hexamethyleneimine with acetylene [5] in presence of caustic

TABLE 1

N-Alkylhexamethyleneimines

N-Alkylhexa-methyleneimine	Yield (%)	Boiling point	d_{20}^{20}	n_D^{20}
N-Ethylhexamethyleneimine	41	150—151°	0.8494	1.4579
N-n-Propylhexamethyleneimine	55	176—177	0.8417	1.4555
N-n-Butylhexamethyleneimine	75	196—197	0.8432	1.4573
N-Isobutylhexamethyleneimine	33	185—186	0.8349	1.4530
N-Isoamylhexamethyleneimine	77	208—209	0.8417	1.4569
N-Benzylhexamethyleneimine	77	127—130 (2 mm)	0.9657	1.5300
N-Allylhexamethyleneimine	53	175—176	0.8626	1.4670
N-β-Hydroxyethylhexamethyleneimine	24	97 (14 mm)	0.9813	1.4853

potash and hydroquinone under a pressure of 16-19 atm. at 145-155°; the reaction gave a resin which was not subjected to investigation.

EXPERIMENTAL

Reaction between hexamethyleneimine and alkyl halides was performed in a three-necked flask fitted with reflux condenser, stirrer and dropping funnel. In the flask were placed 0.5 mole hexamethyleneimine and 100 ml dry benzene, and 0.25 mole alkyl bromide was introduced dropwise while stirring. Chloro derivatives were used in the synthesis of N-benzylhexamethyleneimine and N-β-hydroxyethylhexamethyleneimine. 0.45 mole ethyl bromide was taken for the synthesis of N-ethylhexamethyleneimine.

Molecular weights of the N-alkylhexamethyleneimines, found by titration with 0.1 N HCl, are listed in Table 2.

TABLE 2

Molecular Weights of N-Alkylhexamethyleneimines

N-Alkylhexamethyleneimine	Molecular weight	
	found	calculated
N-Ethylhexamethyleneimine	129.2, 129.4	127.1
N-n-Propylhexamethyleneimine	142.0, 143.0	141.3
N-n-Butylhexamethyleneimine	156.0, 156.5	155.3
N-Isobutylhexamethyleneimine	155.0, 156.0	155.3
N-Isoamylhexamethyleneimine	170.0, 170.0	169.3
N-Benzylhexamethyleneimine	190.5, 191.0	189.3
N-Allylhexamethyleneimine	140.5, 141.3	139.3

SUMMARY

Eight N-alkyl derivatives of hexamethyleneimine were synthesized by reaction of hexamethyleneimine with halogenated derivatives.

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THE KETOVINYLATION OF THIOPHENOLS

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A fairly large number of reactions are known that lead to substitution of a chlorine atom in β-chlorovinyl ketones; on these is based the introduction of the R−CO CH=CH− residue into the molecule of an organic or inorganic compound (the ketovinylation reaction) [1-5]. Up to now, however, the reaction of β-chlorovinyl ketones with sulfur compounds has remained unknown. The present work is devoted to a study of the first example of this type of reaction−that of β-chlorovinyl ketones with thiophenols.

The investigation showed that this reaction goes smoothly when the two components are in aqueous alkaline solution, just as is the case in the ketovinylation of phenols [6].

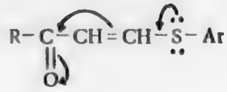
$$RCOCH{=}CHCl + ArSH \xrightarrow{NaOH} RCOCH{=}CHSAr$$
$$R = CH_3,\ n\text{-}C_3H_7,\ C_6H_5;\quad p = C_6H_5,\ p\text{-}CH_3C_6H_4,\ p\text{-}NO_2C_6H_4.$$

Consequently, in the ketovinylation of thiophenols, sodium thiophenate actually reacts and the reaction involves nucleophilic substitution of a chlorine atom in the molecule of β-chlorovinyl ketone under the action of the thiophenate ion.

The reaction is fairly general in character. On the one hand alkyl- and aryl-β-chlorovinyl ketones undergo the reaction, and on the other hand thiophenol itself, its homologs (p-thiocresol) and its derivatives (p-nitrothiophenol). Ketovinylation of thiophenols goes in the cold with great facility, as evidenced by the high yields of reaction products which approach the theoretical in the majority of cases. It is necessary to point out that this reaction proceeds with greater facility than the analogous chlorovinylation of phenols [6], as was to be anticipated in view of the higher nucleophilic activity of the thiophenate ion.

The aryl-β-acylvinyl sulfides RCOCH=CHSAr obtained in the reaction are colorless solids and are easily separated from the reaction mixture by the usual methods. Phenyl-β-butyroylvinyl sulfide is a high-boiling liquid. All the sulfides are fairly stable in storage.

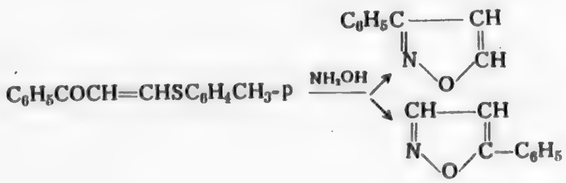
It was a matter of interest to compare the behavior of this new class of compounds with their analogs containing other heteroatoms in the β-position of the ketovinyl residue: β-phenoxyvinyl ketones, β-dialkylaminovinyl ketones and the β-chlorovinyl ketones themselves. The double bond in the prepared compounds is evidently not very active since the compounds could not be made to undergo the diene synthesis even with the extremely active cyclopentadiene. Under mild conditions the ketovinyl sulfide is recovered unchanged, and at higher temperatures (120-150°) the reaction mixture is completely resinified. Consequently, in respect of the dienophilic activity of their double bond, the aryl-β-acylvinyl sulfides are inferior not only to the chlorovinyl ketones [7, 8] but also to the phenoxyvinyl ketones [9], and they approximate to the β-dialkylaminovinyl ketones which are quite incapable of undergoing the diene synthesis [10]. The most probable cause of this behavior is that the conjugation of the free electron pairs of the heteroatom of the β-substituted vinyl ketone with the double bond is more strongly developed in the case of sulfur than in the case of chlorine or oxygen.



As we know, the free electron pairs of the atom of divalent sulfur are readily available for sharing (being inferior in this respect only to the nitrogen atom), as demonstrated by the formation of sulfonium compounds. The high degree of conjugation in the molecule of the prepared ketovinyl sulfides is also evidenced by the high exaltation of the molecular refraction of the only liquid among the prepared compounds—phenyl-β-butyroyl-vinyl sulfide.

The keto group of aryl-β-acylvinyl sulfides manifests its usual properties, retaining the ability to form dinitrophenylhydrazones. It is interesting to note that the latter do not cyclize to pyrazole derivatives under the conditions of formation as sometimes happens in the reaction of 2,4-dinitrophenylhydrazine with α, β unsaturated ketones [11, 12].

In other cases, however, the derivatives undergo a cyclization at the carbonyl group which is characteristic of β-substituted vinyl ketones with formation of a heterocyclic system [1]. Thus, the reaction of p-tolyl-β-benzoylvinyl sulfide with hydroxylamine leads at once to phenylisoxazole in the form of a mixture of approximately equal parts of α- and γ-isomers.



This reaction illustrates the lability of the thiophenoxy group in the compounds studied. Its course is similar to that of reactions of the labile chlorine atom and of active phenoxy and dialkylamino groups in analogous systems (β-chlorovinyl ketones, β-phenoxyvinyl ketones and β-dialkylaminovinyl ketones). The lability of the carbon-sulfur bond in aryl-β-acylvinyl sulfides is also demonstrated by the hydrolysis of the latter with formation of thiophenol on heating with water both in an acidic and in an alkaline medium.

Further study of the reactions of the compounds that we synthesized is now in progress and is of great interest for the synthesis of new types of sulfur-containing unsaturated compounds.

EXPERIMENTAL

Phenyl-β-acetylvinyl sulfide. 29 g thiophenol was dissolved in aqueous alkali (13 g sodium hydroxide in 26 ml water), another 26 ml water was added, and 27.4 g methyl-β-chlorovinyl ketone was added to the solution with stirring. The mixture was stirred 5 hours, the top oily layer was separated and the aqueous layer extracted with ether. The extracts were combined with the main portion of product, washed with 1% sodium hydroxide solution and then with water, and dried over sodium sulfate; the ether was driven off and the residue distilled in vacuum to give 26 g (55%) substance with b.p. 126-129° at 2 mm; it crystallized completely on standing; m.p. 30°.

Found %: C 67.54, 67.33; H 5.93, 5.85; S 18.02, 17.87. $C_{10}H_{10}OS$. Calculated %: C 67.36; H 5.65; S 17.99.

Colorless crystals, soluble in ether, chloroform, acetone and alcohol; stable when stored.

2,4-Dinitrophenylhydrazone. To a solution of 0.5 g dinitrophenylhydrazine in alcohol acidified with concentrated sulfuric acid was added 0.4 g of the substance. The precipitate was filtered off, washed with alcohol, dried and recrystallized from alcohol. Yield 0.95 g; red crystals with m.p. 136-138°.

Found %: N 15.39, 15.23. $C_{16}H_{14}O_4N_4S$. Calculated %: N 15.55

Phenyl-β-benzoylvinyl sulfide. Similarly prepared from 11.5 g thiophenol and 16.6 g phenyl-β-chlorovinyl ketone. The yellow crystals were filtered, dried and recrystallized from ligroin. Yield 24 g (100%) of yellowish, fine needles with m.p. 79.5-80.5°.

Found %: C 75.43, 75.42; H 5.24, 5.17. $C_{15}H_{12}OS$. Calculated %: C 75.00; H 5.36.

Phenyl-β-butyroylvinyl sulfide. Similarly prepared from 8.1 g thiophenol and 10.1 g propyl-β-chlorovinyl ketone, using 20% aqueous solution of sodium hydroxide. Working-up in the usual manner and distillation in vacuum gave 13.5 g (86%) of a yellowish oil which was stable in storage.

B.p. 126-128° (1 mm), n_D^{20} 1.5922, d_4^{20} 1.0740, MR_D 65.01; calculated 61.64; EMR_D 3.37.

Found %: C 69.46, 69.50; H 6.92, 7.05. $C_{12}H_{14}OS$. Calculated %: C 69.85; H 6.84.

p-Tolyl-β-acetylvinyl sulfide. Similarly prepared from 25.6 g p-thiocresol and 20.5 g methyl-β-chlorovinyl ketone. The resultant precipitate was filtered, washed with water and dried in vacuum over calcium chloride. Yield 37 g (100%); recrystallization from ligroin gave colorless crystals with m.p. 60.5-61.5°.

Found %: C 68.59, 68.49; H 6.55, 6.47. $C_{11}H_{12}OS$. Calculated %: C 68.69; H 6.29.

p-Tolyl-β-benzoylvinyl sulfide. Similarly prepared from 7.8 g p-thiocresol and 10 g phenyl-1-chlorovinyl ketone. Working-up in the usual fashion gave 18.3 g (100%) of substance; recrystallization from ligroin gave yellowish crystals with m.p. 85.5-86.5°.

Found %: 75.23, 75.43; H 5.74, 5.73. $C_{16}H_{14}OS$. Calculated %: C 75.63; H 5.55.

p-Nitrophenyl-β-benzoylvinyl sulfide. Similarly prepared from 4.7 g p-nitrophenol and 5.3 g phenyl-β-chlorovinyl ketone. Working-up in the usual manner and recrystallization from alcohol gave 8.5 g (100%) of substance in the form of yellow needles with m.p. 138-138.5°.

Found %: C 62.99, 63.15; H 4.16, 4.16. $C_{15}H_{11}O_3NS$. Calculated %: C 63.13; H 3.89.

Reaction of p-tolyl-β-benzoylvinyl sulfide with hydroxylamine. To a solution of 12.7 g p-tolyl-β-benzoylvinyl sulfide in 150 ml methanol was gradually added 4.2 g hydroxylamine hydrochloride in 50 ml methanol. The mixture was heated on a water bath for 8 hours, left overnight and then poured into water.

The separated oil was extracted with ether, the extracts were dried over magnesium sulfate, the ether was driven off and the residue was distilled in vacuum. Yield 3.5 g (48%) of phenylisoxazole with the following constants: b.p. 81-83° at 1 mm, n_D^{20} 1.5822, d_4^{20} 1.1370, MR_D 42.61; calculated 42.61.

Literature data for phenylisoxazole [12]: b.p. 156-158° at 25 mm.

Treatment of the product with sodium alkoxide by the Claisen procedure [13] resulted in formation from 1.73 g of phenylisoxazole of 0.98 g ω-cyanoacetophenone with m.p. 78°, equivalent to an α-isomer content of 57%.

Hydrolysis of p-tolyl-β-acetylvinyl sulfide in an acid medium. 1.5 g of p-tolyl-β-acetylvinyl sulfide was heated on a water bath for 24 hours with 50 ml 20% aqueous sodium hydroxide solution. After steam distillation, 1.1 g of the characteristic yellow precipitate of lead thiophenate was isolated from the distillate.

SUMMARY

1. A method was developed for the synthesis of previously unknown aryl-β-acylvinyl sulfides; the latter were obtained in high yields by reaction of β-chlorovinyl ketones with thiophenols in an alkaline medium.

2. Some reactions of these compounds were investigated and showed their close similarity to other β-substituted vinyl ketones.

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SOME β-AMINO ACIDS OF THE THIOPHENE SERIES

V. P. Mamaev and T. D. Rubina

The study of β-amino acids of the heterocyclic series has been neglected due to their difficult accessibility; definite interest is therefore attached to the preparation of these acids and their derivatives. It is known that one of the most general as well as one of the simplest methods of synthesis of β-amino acids is the method of V. M. Rodionov, based on the reaction of aldehydes with malonic acid in presence of alcoholic ammonia [1]. Subsequently it was established that higher yields of β-aryl-β-amino acids are obtained if the ammonia is replaced by ammonium acetate [2]. The most readily accessible of the β-amino acids of the heterocyclic series was found to be β-(2-thienyl)-β-aminopropionic acid. The latter is easily prepared by Rodinov's method starting from α-thiophenealdehyde [3].

In the present work we applied this method to the synthesis of β-(3-thienyl)-β-aminopropionic (I) and β-(2-ethyl-5-thienyl)-β-aminopropionic acid (II) from β-thiophenealdehyde (III) and 2-ethyl-5-thiophenealdehyde (IV) respectively. Apart from the β-amino acids, β-(3-thienyl)-acrylic and β-(2-ethyl-5-thienyl)-acrylic (VI) acids were isolated. In both cases we conducted the reaction of the aldehydes with malonic acid in presence of ammonium acetate, previous work [3] having established that the maximum yield of β-amino acid is obtained under these conditions.

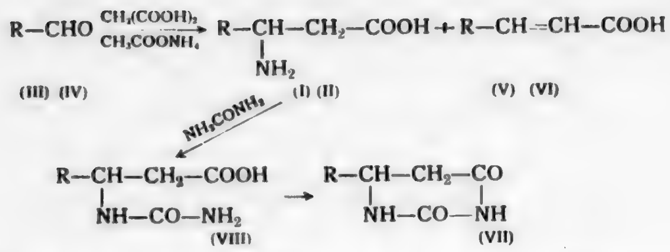
It is necessary to point out that the formation of β-amino acid from β-thiophenealdehyde goes with greater facility than from α-thiophenealdehyde. The reaction period in the former case is shorter and the yield of β-amino acid higher (6 hours instead of 10 hours; yields 54.7 and 42.7%). It is interesting to compare this observation with the report in the literature that β-thiophenecarboxylic acid amide is readily transformed into amine by Hofmann's method, whereas α-thiophenecarboxylic acid amide does not form an amine under these conditions [4]. Substituents in the β-position of the thiophene ring in some cases evidently possess greater reactivity than substituents in the α-position.

The starting aldehydes were synthesized in the following manner: 2-ethyl-5-thiophenealdehyde was obtained by formylation of α-ethylthiophene with N-methylformanilide in presence of phosphorus oxychloride [5], while β-thiophenealdehyde was prepared from β-methylthiophene by bromination of the latter with N-bromosuccinimide to 3-bromomethylthiophene followed by transformation of the $-CH_2Br$ group into the aldehyde group [6]. We prepared β-methylthiophene from α-bromopropionic ester and cyanoacetic ester by the method previously described [7].

The benzoyl derivatives were prepared for the purpose of characterization of the synthesized β-amino acids. We expected to obtain the corresponding β-ureido acid by heating an aqueous solution of β-(3-thienyl)-β-aminopropionic acid with urea; judging, however, by the analysis and the high melting point (248°) the product formed is 6-(3'-thienyl)-2,4-dioxohexahydropyrimidone (VII), i.e. under the experimental conditions the ureido acid formed (VIII) loses a molecule of water and is transformed into a derivative of dihydrouracil.

EXPERIMENTAL

<u>β-(3-Thienyl)-β-aminopropionic acid (I).</u> A solution of 1.12 g β-thiophenealdehyde, 1.06 g malonic acid and 1.59 g ammonium acetate in 2.2 ml alcohol was boiled on a water bath for 6 hours. After cooling, the β-amino acid was filtered off and washed first with warm alcohol and then with ether. Yield 0.92 g (54.7%); m.p. 201.5-202° (with decomp.). Dilution of the alcoholic filtrate with water led to separation of β-(3-thienyl)-acrylic acid. Yield 0.14 g (10.6%). M.p. 149-150° (from aqueous alcohol).



For I, III, V and VIII R = 3-thienyl-; for II, IV and VI R = 2-ethyl-5-thienyl-.

Found %: C 54.64, 54.75; H 3.75, 3.88. $C_7H_6O_2S$. Calculated %: C 54.53; H 3.92.

The β-amino acid was purified by dissolving 0.1 g in 4.5 ml water to which was added 2 drops of concentrated hydrochloric acid. The solution was evaporated to dryness on a water bath. The residue was dissolved in a small quantity of hot alcohol and the hydrochloride of the β-amino acid was then brought down with ether. The β-amino acid was precipitated from the aqueous solution of the pure hydrochloride by a saturated solution of sodium acetate. M.p. 203° (with decomp.).

Found %: N 8.39, 8.49. $C_7H_9O_2NS$. Calculated %: N 8.19.

Hydrochloride: m.p. 187.5-188° (with decomp.).

Found %: N 6.68, 6.78. $C_7H_{10}O_2NSCl$. Calculated %: N 6.75.

N-Benzoyl-β-(3-thienyl)-β-aminopropionic acid. To an aqueous solution of 0.1 g of the β-amino acid was added (with cooling) 1 ml of 10% sodium hydroxide solution and then 0.1 ml benzoyl chloride. The mixture was stirred 2 hours, filtered and acidified; the precipitate was separated and washed with water. Yield of benzoyl derivative 0.09 g (66.6%). M. p. 188-188.5° (from water).

Found %: N 5.09, 4.98. $C_{14}H_{13}O_3NS$. Calculated %: N 5.09.

6-(3'-Thienyl)-2, 4-dioxohexahydropyrimidine [6-(3'-thienyl)-dihydrouracil]. A solution of 0.35 g β-(3-thienyl)-β-aminopropionic acid and 1.62 g urea in 8.2 ml water was heated 17 hours on a water bath. After cooling, the solution was filtered and treated with ether for removal of impurities. The aqueous layer was acidified; after standing for many days a light brown precipitate came down. Yield 0.29 g, m.p. 248° (from aqueous alcohol).

Found %: N 14.39, 14.53. $C_8H_8O_2N_2S$. Calculated %: N 14.35

β-(2-Ethyl-5-thienyl)-β-aminopropionic acid (II). A mixture of 6.25 g 2-ethyl-5-thiophenealdehyde, 4.75 g malonic acid, 7.2 g ammonium acetate and 10 ml alcohol was heated on a water bath for 5 hours; a further 9.2 g ammonium acetate was then added and the heating continued for another 9 hours. The precipitate of β-amino acid, separating after cooling and prolonged standing, was filtered and washed with alcohol and ether. Yield 2.7 g (30.4%); m.p. 196-197° (with decomp.). After purification by reprecipitation (as in the case of the preceding amino acid) the m.p. was 198-199° (with decomp.).

Found %: C 54.56, 54.32; H 6.46, 6.54; N 6.88, 6.93. $C_9H_{13}O_2NS$. Calculated %: C 54.27; H 6.53; N 7.03.

The alcoholic mother liquor was diluted with water and a resinous mass separated out and was distilled with steam to remove impurities. The oil remaining in the distillation flask crystallized on standing. The solid was collected and recrystallized first from iso-octane and then from dilute acetic acid. Yellowish crystals with m.p. 97-99°.

Found %: C 59.71, 59.53; H 5.85, 5.80. $C_9H_{10}O_2S$. Calculated %: C 59.34; H 5.49.

N-Benzoyl-β-(2-ethyl-5-thienyl)-β-aminopropionic acid was obtained by the method used for the preceding benzoyl derivative. M.p. 183-183.5° (from aqueous alcohol).

Found %: N 4.79, 4.90. $C_{16}H_{17}O_3NS$. Calculated %: N 4.62.

SUMMARY

V. M. Rodionov's method was used for the synthesis of β-(3-thienyl)-β-aminopropionic acid and β-(2-ethyl-5-thienyl)-β-aminopropionic acid. In this way it was established that the Rodionov reaction can be used for the preparation of β-amino acids of the thiophene series.

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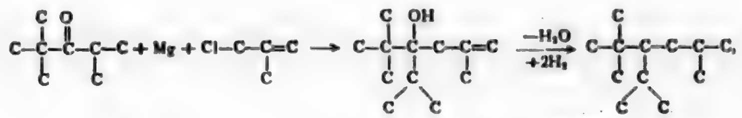
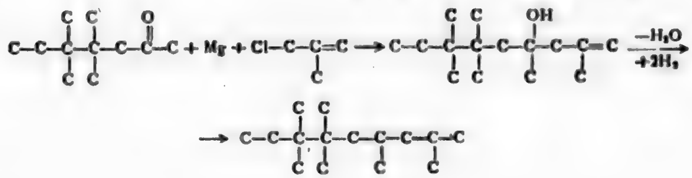
THE SYNTHESIS OF BRANCHED ALIPHATIC HYDROCARBONS OF COMPOSITION $C_{10} - C_{15}$ BY THE GRIGNARD AND GRIGNARD-WURTZ REACTIONS

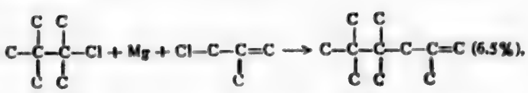
A. D. Petrov, V. L. Sushchinsky, E. P. Zakharov and T. I. Rogozhnikova

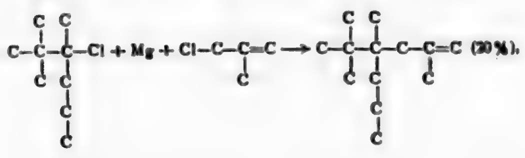
It has been shown in previous communications [1] that, in contrast to isobutyl magnesium halides, isobutenyl magnesium halides react with esters of monobasic and dibasic acids in the normal way. In a continuation of this work, we have established in the present study that a halide of the allyl type also reacts in the normal way even with highly branched ketones, as can be seen from equations 1 and 2. This circumstance makes the above reaction a convenient method for the preparation of branched hydrocarbons with one or two quaternary carbon atoms.

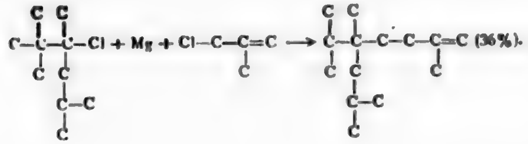
1) 

2) 

In the same communications [1] it has been shown that whereas a symmetrical chloride with two adjacent quaternary carbon atoms (2, 2, 3-trimethyl-3-chlorobutane) reacts with methylallyl chloride in the presence of magnesium (according to Yavorsky) giving low yield (6.5%), its asymmetric analogs react with allyl halides giving considerably higher yields (20-35%).

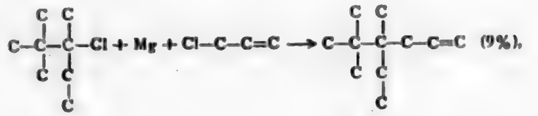
3) 

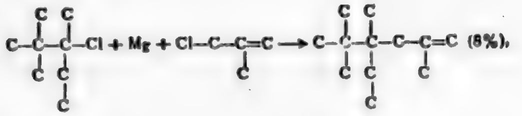
4) 

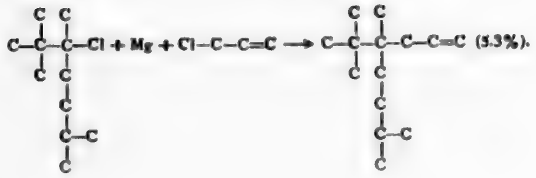
5) 

With the aim of finding the reason for this interesting phenomenon, and also of studying the influence of the nature of the halide, the structure of the radical, and the conditions of the condensation (whether carried out according to Yavorsky or Grignard) on the yields of the aliphatic hydrocarbons, we have carried out in the present work a large number of condensation reactions, represented by equations 6-23.

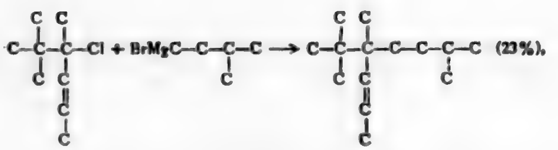
Yavorsky's method (the condensation of saturated alkyl halides with unsaturated):

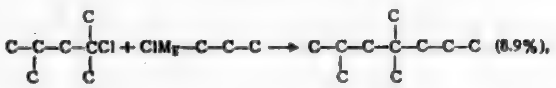
6) 

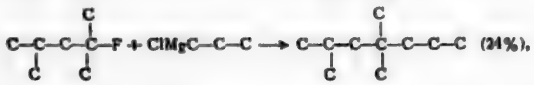
7) 

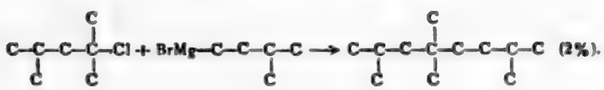
8) 

Grignard's method:

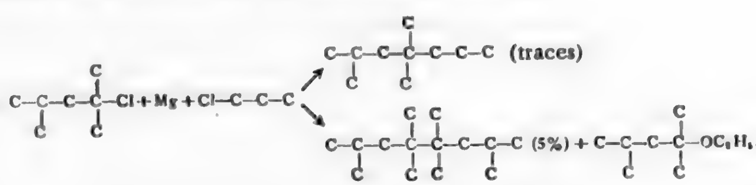
9) 

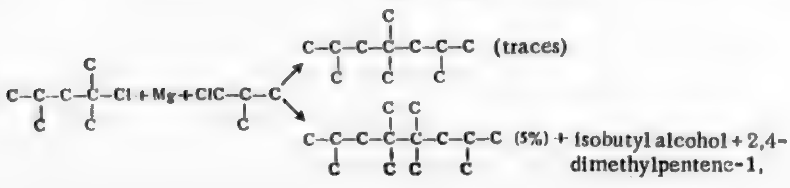
10) 

11) 

12) 

Yavorsky's method (the condensation of two saturated alkyl halides):

13) 

14) 

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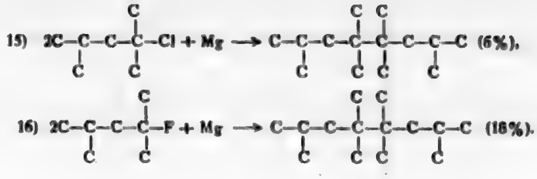
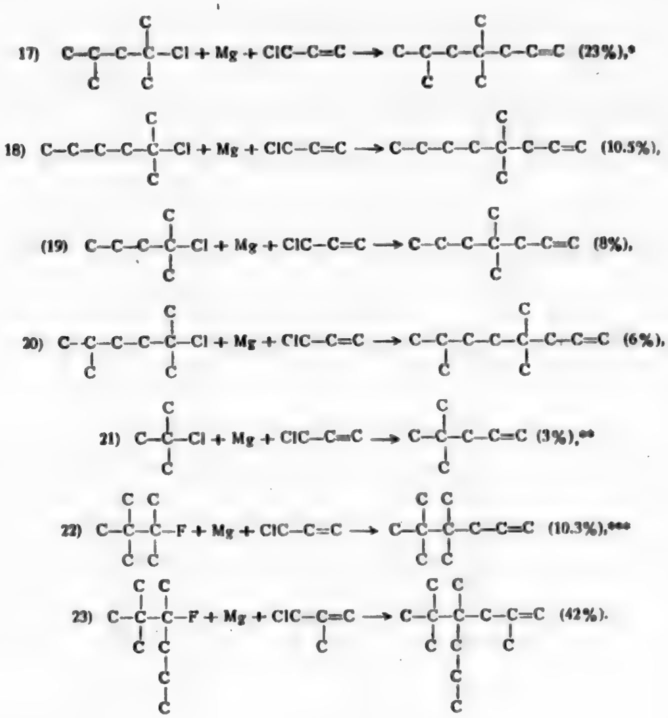


Yavorsky's method (the condensation of saturated alklyl halides with unsaturated):



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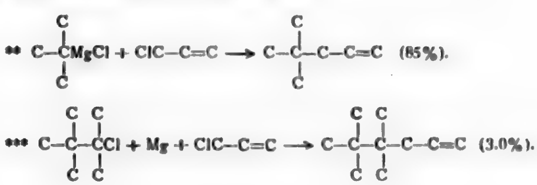
* Yield 3 times greater than by the Grignard reaction (no. 10).



Examination of the data given leads to the following conclusions. A comparison of reactions 10 and 11, 15 and 16, 22 and 3, 23 and 4 leads to the conclusion that the condensation of allyl halides with different tertiary fluorides gives yields which are 3 times greater than those obtained using the corresponding chlorides. The higher yields in the case of the fluorides are evidently explained for the most part by their greater activity, which results from the fact that the energy of the C-F bond equals 102 cal., whereas the energy of the C-Cl bond equals 78 cal.

The caracterization of the nature of the influence of the structure of the reacting radicals on the yields is a more difficult problem. The inductive effect undoubtedly plays a certain part in this (the gradual increase in the yields in reactions 6, 4, 5, and also in 19, 18 and 17). The sudden fall in yield in reactions 8 and 20, and the maximum values of the yields in reactions 5 and 17, however, lead to the suggestion that the presence of conjugated simple bonds in the saturated tertiary alkyl halide, or, in other words, the presence of a polarization between carbon atoms 3 and 4 as a result of the structure, has a certain influence on the raising of the yields.

It seems to us that the high yield in the case of the isobutyl radical is explained by the mobility of the chlorine atom, which is caused by the coincidence of the inductive effects of the chlorine and the two methyl groups. With the propyl radical we have the influence of only one methyl group, and in the isoamyl radical the methyl groups are too far from the chlorine to strengthen the inductive effect of the latter.

When σ, σ-conjugation is present in the saturated halides their reactivity, as can be seen from the data given, is close to the reactivity of the halides with σ, π-conjugation. When condensations by the Grignard and Yavorsky methods are compared we see that in some reactions (see 10 and 13) the first is preferable and in other cases the second.

It is interesting to note that it is possible to condense 2-chloro-2, 4-dimethylpentane into a hydrocarbon with two adjacent quaternary carbon atoms and that this can be done with a yield twice as great as in the case of tert-butyl chloride (as is known, Levina [2] was not able to carry out the condensation of 2-chloro-2, 4-dimethylpentene-3 because of the quantitative removal of hydrogen chloride from this halide). It should be noted that the condensation, conditionally called Yavorsky condensation (i.e. the simultaneous pouring on to magnesium), of two different saturated alkyl halides usually takes place anomalously (see 13 and 14).

EXPERIMENTAL

In the present work we do not give the course of the synthesis, since this has been described earlier [1, 3 etc.]. We give here only a short outline of the synthesis of each hydrocarbon with the percentage yield and the properties of the compounds obtained (including the intermediate products). The starting materials were taken in such amount that 0.5-1 mole of reagent was obtained for the last main reaction. The sequence of the description corresponds to the arrangement of the reactions in the general part.*

I. 2, 2, 5-Trimethyl-3-isopropylhexane. Reagents: tert-butyl chloride, magnesium and isobutyryl chloride, isobutenyl chloride and magnesium; hydrogen (hydrogenation over nickel); sodium acetate and acetic anhydride (dehydration); hydrogen (hydrogenation over palladium).

Intermediate compounds. a) 2, 4, 4-Trimethylpentanone-3. Yield 63.5%; b.p. 134-136° (745 mm), n_D^{20} 1.4047, d_4^{20} 0.8052; oxime, m.p. 138-140°. According to [4]: b.p. 134-135°, n_D^{20} 1.40513, d_4^{20} 0.8054; oxime, m.p. 139-140° [5].

b) 2, 5, 5-Trimethyl-4-isopropylhexene-1-ol-4. Yield 61.5%. Not described in the literature. B.p. 80.9° (12 mm), n_D^{20} 1.4590, d_4^{20} 0.8654, MR_D 58.22; calc. 58.67.

Found %: C78.11; H 13.16. $C_{12}H_{24}O$. Calculated %: C 78.08; H 13.21.

c) 2, 2, 5-Trimethyl-3-isopropylhexanol-3. Not described in the literature. B.p. 65.6-66.5° (2 mm), n_D^{20} 1.4506, d_4^{20} d.8552;** MR_D 58.62; calc. 59.14.

Found %: C 77.38; H 14.13. $C_{12}H_{26}O$. Calculated %: C 77.42; H 14.09.

* In the experimental part Roman numerals are used to denote those reactions which in the general part are denoted by Arabic numerals. Here, moreover, only those reactions which have not been discussed up to the present are considered.

** As in original — Publisher's note.

d) 2, 2, 5-Trimethyl-3-isopropylhexene-3. Not described in the literature. B.p. 49° (6 mm), n_D^{20} 1.4432, d_4^{20} 0.7806, MR_D 57.18; calc. 57.14.

Found %: C 85.37; H 14.45. $C_{12}H_{24}$. Calculated %: C 85.64; H 14.37.

Products of oxidation (by $KMnO_4$ in aqueous medium). 2, 2, 4-Trimethylpentanone-3. B.p. 133-136° (745 mm), n_D^{20} 1.4047, d_4^{20} 0.8052, oxime, m.p. 138-140° (from alcohol). Literature data [4, 5]: b.p. 134-135°, n_D^{20} 1.40513, d_4^{20} 0.8054; oxime, m.p. 139-140°.

Isobutyric acid, b.p. 152-155° (748 mm); anilide, m.p. 104-105° (from alcohol). According to [6]: melting point of anilide 105°.

2, 2, 5-Trimethyl-3-isopropylhexane. Not described in the literature. Yield 89%; b.p. 182.6° (749 mm), n_D^{20} 1.4294, d_4^{20} 0.7669, MR_D 57.30; calc. 57.60.

Found %: C 84.70; H 15.18. $C_{12}H_{26}$. Calculated %: C 84.71; H 15.29.

Raman spectrum λ (cm^{-1}): 252 (2); 317 (1); 440 (3); 476 (2); 500 (1); 534 (4); 595 (2 broad); 640 (2); 695 (3); 762 (4); 798 (1); 830 (6); 890 (0); 927 (4 broad); 956 (4 sharp); 1006 (3); 1039 (3 broad); 1081 (1); 1117 (3 broad); 1175 (2); 1196 (2); 1219 (3); 1237 (2 broad); 1256 (2); 1313 (4); 1354 (3 broad); 1396 (1); 1453 (10); 1472 (10).

II. 2, 4, 6, 6, 7, 7-Hexamethylnonane. Reagents: ethyl bromide, acetone and Mg, dry HCl, Mg and mesityl oxide, Mg and isobutenyl chloride, CH_3COONa and $(CH_3CO)_2O$ (dehydration); H_2 (hydrogenation over Ni); H_2 (hydrogenation over Pd).

Intermediate compounds. a) 2 Methylbutanol-2. Yield 64%; b.p. 100.5-101° (750 mm), n_D^{20} 1.4056, d_4^{20} 0.8087; according to [7, 8]: b.p. 102°; n_D^{20} 1.4052, d_4^{20} 0.809.

b) 2-Methyl-2-chlorobutane. Yield 81%; b.p. 85.7°, n_D^{20} 1.4069, d_4^{20} 0.8706; according to [8]: b.p. 86°, n_D^{20} 1.407, d_4^{20} 0.8692.

c) 4, 4, 5, 5-Tetramethylheptanone-2. Yield 5%; b.p. 120.5° (36 mm), n_D^{20} 1.4702, d_4^{20} 0.8969, MR_D 52.98; calc. 53.01. 2, 4-Dinitrophenylhydrazone, m.p. 114°; according to [9]: b.p. 118-120° (35 mm), n_D^{20} 1.4620-1.4625; 2, 4-dinitrophenylhydrazone, m.p. 114°.

Found %: C 77.60; H 13.10. $C_{11}H_{22}O$. Calculated %: C 77.58; H 13.03.

d) 2, 4, 6, 6, 7, 7-Hexamethylnonene-1-ol-4. Yield 50%. Not described in the literature. B.p. 100-102° (2 mm), n_D^{20} 1.4835, d_4^{20} 0.9022, MR_D 71.73; calc. 72.52.

Found %: C 79.43; H 13.42. $C_{15}H_{30}O$. Calculated %: C 79.57; H 13.36.

e) 2, 4, 6, 6, 7, 7-Hexamethylnonadiene-1, 3. Yield 82.5%. Not described in the literature. B.p. 78° (2 mm), n_D^{20} 1.4779, d_4^{20} 0.8323, MR_D 70.53; calc. 70.8.

Found %: C 86.42; 86.48; H 13.52, 13.58. $C_{15}H_{28}$. Calculated %: C 86.47; H 13.53.

Products of oxidation (by $KMnO_4$ in aqueous medium): 4, 4, 5, 5-tetramethylheptanone-2; 2, 4-dinitrophenylhydrazone, m.p. 114°.

Found %: N 16.08, 16.06. $C_{17}H_{26}O_4N_4$. Calculated %: N 15.99; formic acid (b.p. 98-106°, precipitate of mercurous chloride from mercuric chloride solution); pyruvic acid (m.p. 13-14°, n_D^{20} 1.4342, d_4^{20} 1.2660; silver salt).

Found %: Ag 56.06, 55.92. $C_3H_3O_3Ag$. Calculated %: Ag 55.34; 2, 4-dinitrophenylhydrazone, m.p. 216-218°.

Found %: N 21.12, 21.02. $C_9H_8O_6N_4$. Calculated %: N 20.89.

Literature data [10, 11]: melting point of pyruvic acid 13.6°, n_D^{15} 1.4302, d_4^{15} 1.267; 2, 4-dinitrophenylhydrazone, m.p. 218°.

f) 2, 4, 6, 6, 7, 7-Hexamethylnonene-3. B. p. 97.5° (11 mm), n_D^{20} 1.4551, d_4^{20} 0.8169, MR_D 70.90; calc. 69.27.

Found %: C 85.55, 85.66; H 14.61, 14.99. $C_{15}H_{30}$. Calculated %: C 85.63; H 14.37.

Products of oxidation (by $KMnO_4$ in aqueous medium): 4, 4, 5, 5-tetramethylheptanone-2 [b.p. 122-124° (42 mm); 2, 4-dinitrophenylhydrazone, m.p. 114°]; isobutyric acid (b.p. 153-156°; anilide, m.p. 104-105°).

2, 4, 6, 6, 7, 7-Hexamethylnonane. Not described in the literature. B. p. 94-94.6° (16 mm), n_D^{20} 1.4510, d_4^{20} 0.8028, MR_D 71.24; calc. 71.27.

Found %: C 84.52, 84.34; H 15.00, 15.16. $C_{15}H_{32}$. Calculated %: C 84.91; H 15.09.

VI. 4, 5, 5-Trimethyl-4-ethylhexene-1. Reagents: ethyl bromide, magnesium and pinacolone; dry HCl; allyl chloride and Mg.

Intermediate compounds. a) 2, 2, 3-Trimethylpentanol-3. Yield 46%; b.p. 67.8-68.9° (33.5 mm), n_D^{20} 1.4352, d_4^{20} 0.8310. According to [12]: yield 38%; b.p. 68-70° (35 mm), n_D^{20} 1.4352.

b) 3-Chloro-2, 2, 3-trimethylpentane. Not described in the literature. Yield 77.7%; b.p. 70.5-71° (40 mm); n_D^{20} 1.4445, d_4^{20} 0.9069, MR_D 43.64; calc. 44.01.

Found %: Cl 24.12, 24.16. $C_8H_{17}Cl$. Calculated %: Cl 23.85.

4, 5, 5-Trimethyl-4 ethylhexene-1. Not described in the literature. Yield 8.9%; b.p. 59° (12 mm), n_D^{20} 1.4403, d_4^{20} 0.7834, MR_D 52.23; calc. 52.53.

Found %: C 85.41, 85.36; H 14.34, 14.42. $C_{11}H_{22}$. Calculated %: C 85.62; H 14.38.

Hydrogenated to 2, 2, 3-trimethyl-3-ethylhexane. Not described in the literature. Yield 90%; b.p. 176.5-177° (739 mm); freezing point −110° (glass), n_D^{20} 1.4386, d_4^{20} 0.7786, MR_D 53.12; calc. 53.00.

Found %: C 83.69, 83.81; H 15.67, 15.40. $C_{11}H_{24}$. Calculated %: C 84.55; H 15.45.

VII. 2, 4, 5, 5-Tetramethyl-4-ethylhexene-1. Not described in the literature. Reagents: 3-chloro-2, 2, 3-trimethylpentane (see previous synthesis), isobutenyl chloride and magnesium. Yield 8%.

B. p. 71° (7 mm), n_D^{20} 1.4513, d_4^{20} 0.8011, MR_D 56.61; calc. 57.15.

Found %: C 85.66, 85.59; H 14.32, 14.40. $C_{12}H_{24}$. Calculated %: C 85.62; H 14.38.

Hydrogenated over Ni to 2, 2, 3, 5-tetramethyl-3-ethylhexane. Not described in the literature. B. p. 192.5-193° (750 mm); freezing point −108° (glass), n_D^{20} 1.4405, d_4^{20} 0.7862, MR_D 57.17; calc. 57.62.

Found %: C 83.74, 83.92; H 15.69, 15.45. $C_{12}H_{26}$. Calculated %: C 84.61; H 15.39.

Raman spectrum λ (cm^{-1}): 250 (3); 290 (2 broad); 668 (4); 700 (2); 736 (2); 838 (4); 845 (4); 890 (3); 927 (4); 964 (2 broad); 996 (1); 1030 (4 broad); 1110 (3 broad); 1198 (1); 1228 (4); 1308 (1); 1352 (2); 1456 (6 broad); 1470 (5 broad).

VIII. 4, 7-Dimethyl-4-tert-butyloctene-1. Reagents: isopropyl bromide, ethylene oxide and magnesium; 40% hydrobromic acid and H_2SO_4 (d 1.84); pinacolone and Mg; dry HCl; allyl chloride and Mg.

Intermediate compounds. a) 3-Methylbutanol-1. Yield 52%; b.p. 130-131° (747 mm), n_D^{20} 1.4058, d_4^{20} 0.8138.

b) Isoamyl bromide. Yield 50%; b.p. 42.5° (45 mm), n_D^{20} 1.4410, d_4^{20} 1.2088, MR_D 33.06; calc. 33.00.

c) 2, 2, 3, 6-Tetramethylheptanol-3. Yield 52%; b.p. 69.2-71.3° (3 mm), n_D^{20} 1.4387, d_4^{20} 0.8506, MR_D 53.25; calc. 54.52.

Found %: C 76.42, 76.58; H 14.01, 14.06. $C_{11}H_{24}O$. Calculated %: C 76.67; H 14.04.

d) 3-Chloro-2, 2, 3, 6-tetramethylheptane. Not described in the literature. Yield 51%; b.p. 62.6-63° (3 mm), n_D^{20} 1.4468, d_4^{20} 0.8841, MR_D 57.62; calc. 57.87.

Found %: C 18.12, 18.27. $C_{11}H_{23}Cl$. Calculated %: Cl 18.59.

4, 7-Dimethyl-4-tert-butyloctene-1. Not described in the literature. Yield 5.3%; b.p. 57-58° (2 mm), n_D^{20} 1.4370, d_4^{20} 0.7760; MR_D 66.52; calc. 66.39.

Found %: C 85.38, 85.46; H 14.16, 14.39. $C_{14}H_{28}$. Calculated %: C 85.62; H 14.38.

Hydrogenated over Ni to 4, 7-dimethyl-4-tert-butyloctane. Not described in the literature. Yield 80%; b.p. 54° (2 mm), freezing point −110° (glass), n_D^{20} 1.4316, d_4^{20} 0.7704, MR_D 66.73; calc. 66.85.

Found %: C 84.53, 84.60; H 15.20, 15.29. $C_{14}H_{30}$. Calculated %: C 84.75; H 15.24.

IX. 4, 7-Dimethyl-4-tert-butyloctene-2. Reagents: pinacolone, allyl chloride and Mg; hydrochloric acid (d 1.19); isoamyl bromide and Mg.

Intermediate compounds. a) 4, 5, 5-Trimethylhexene-1-ol-4. Yield 87.3%; b.p. 87° (56 mm), n_D^{20} 1.4465, d_4^{20} 0.8562. According to [3]: b.p. 165-170°, n_D^{20} 1.4452; according to [13]: b.p. 168.4°; n_D^{20} 1.4476, d_4^{20} 0.85508.

b) 4-Chloro-4, 5, 5-trimethylhexene-2. Yield 72%; b.p. 42.7-43° (3 mm), n_D^{20} 1.4546, d_4^{20} 0.9052, MR_D 48.09; calc. 48.16. Literature data [3]: b.p. 46-47° (6 mm), n_D^{20} 1.4567, d_4^{20} 0.9101.

4, 7-Dimethyl-4-tert-butyloctene-2. Not described in the literature. Yield 23%; b.p. 70.4° (35 mm), n_D^{20} 1.4363, d_4^{20} 0.7810, MR_D 66.68; calc. 66.39.

Found %: C 85.82; 85.75; H 14.22, 14.30. $C_{14}H_{28}$. Calculated %: C 85.63; H 14.37.

Oxidation products: acetic acid (b.p. 108-113°, ethyl acetate prepared); the acid $C_{12}H_{24}O_2$ (boiling point above 140°; silver salt: found %: Ag 36.02, 35.93. $C_{12}H_{23}O_2Ag$. Calculated %: Ag 35.12. Anilide, m.p. 13-15°. Found %: N 5.12, 5.09. $C_{18}H_{29}ON$. Calculated %: N 5.09).

Hydrogenated over Ni to 4, 7-Dimethyl-4-tert-butyloctane (see previous synthesis). Yield 76%; b.p. 87° (11 mm), n_D^{20} 1.4315, d_4^{20} 0.7703, MR_D 66.73; calc. 66.85.

Found %: C 84.51, 84.68; H 15.28, 15.35. Calculated %: C 84.76; H 15.24.

X. 2, 4, 4-Trimethylheptane. Reagents: methyl bromide, Mg and methyl isobutyl ketone; dry HCl; propyl chloride and Mg.

Intermediate compounds. a) 2, 4-Dimethylpentanol-2. Yield 76.6%; b.p. 59.5° (42.5 mm), n_D^{20} 1.4170, d_4^{20} 0.8119, MR_D 35.88; calc. 36.05. According to [13]: b.p. 133° (749 mm), n_D^{20} 1.4172, d_4^{20} 0.8158.

b) 2-Chloro-2, 4-dimethylpentane. Yield 89%; b.p. 46° (44 mm), n_D^{20} 1.4182, d_4^{20} 0.8628, MR_D 39.32; calc. 39.39. According to [14]: b.p. 33-34° (20 mm), n_D^{15} 1.4239.

2, 4, 4-Trimethylheptane.* Yield 8.8 ; b.p. 149.5° (753 mm), n_D^{20} 1.4143, d_4^{20} 0.7400, MR_D 48.08; calc. 48.18. Literature data [15]: b.p. 151-152°, n_D^{20} 1.4143, d_4^{20} 0.7346.

XII. 2, 4, 4, 7-Tetramethyloctane. Reagents: 2-chloro-2, 4-dimethylpentane (see previous synthesis), isoamyl bromide and magnesium. Yield 2.1%.

b.p. 183-184° (750 mm), n_D^{20} 1.4232, d_4^{20} 0.7540, MR_D 57.55; calc. 57.62. According to [17]: b.p. 67.5° (13 mm); n_D^{20} 1.4217, d_4^{20} 0.7507.

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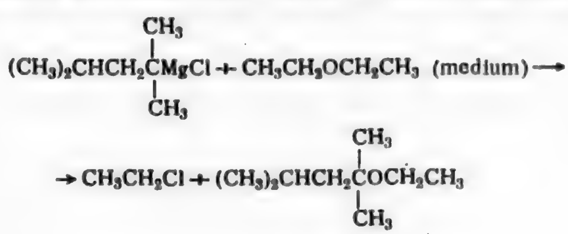
* In an attempt to prepare this hydrocarbon by Yavorsky's method [16] (pouring a mixture of propyl chloride and 2-chloro-2, 4-dimethylpentane on to magnesium), only traces of 2, 4, 4-trimethylheptane were obtained. Two fractions were obtained, which were identified as: 1) ethyl 2, 4-dimethylpentanyl-2 ether, evidently from the reaction:



XIV. 2, 4, 4, 6-Tetramethyloctane. Reagents: 2-chloro-2, 4-dimethylpentane, isobutyl chloride and magnesium. The reaction was carried out according to Yavorsky [16]. The product of the normal condensation–2, 4, 4, 6-tetramethloctane–was obtained in negligible quantities, and its properties were not determined.

Products: 2, 4, 4, 5, 5, 7-hexamethyloctane (5%); a considerable amount of 2, 4-dimethylpentene-1 (always present in the products of reaction with 2-chloro-2, 4-dimethylpentane) and isobutyl alcohol.

XV. 2, 4, 4, 5, 5, 7-Hexamethyloctane. Reagents: 2-chloro-2, 4-dimethylpentane, allyl chloride and magnesium. Yield 6%. Properties–see the synthesis of 2, 4, 4-trimethylheptane, footnote.

XVII. 4, 4, 6-Trimethylheptene-1. Not described in the literature. Reagents: 2-chloro-2, 4-dimethylpentane, allyl chloride and magnesium. Yield 23.3%.

b.p. 139-140° (737 mm), n_D^{20} 1.4220, d_4^{20} 0.7543, MR_D 47.26; calc. 47.91.

Found %: C 85.25, 85.37; H 14.68, 14.75. $C_{10}H_{20}$. Calculated %: C 85.62; H 14.38.

Hydrogenated over Ni to 2, 4, 4-trimethylheptane. B.p. 150° (753 mm), n_D^{20} 1.4142, d_4^{20} 0.7396. Literature data [15]: see the synthesis of 2, 4, 4-trimethylheptane.

XVIII. 4, 4-Dimethyloctene-1. Reagents: butylchloride, acetone and Mg; dry HCl; allyl chloride and Mg.

Intermediate compounds. a) 2-Methylhexanol-2. Yield 63%; b.p. 69-70° (42.5 mm), n_D^{20} 1.4168, d_4^{20} 0.8150, MR_D 35.84; calc. 36.05. According to [18]: b.p. 139.4-140.4° (735 mm), 53-55° (15 mm), n_D^{20} 1.4175, d_4^{20} 0.8119.

b) 2-Chloro-2-methylhexane. Yield 89%; b.p. 59.5° (52 mm), n_D^{20} 1.4200, d_4^{20} 0.8635, MR_D 39.46; calc. 39.39. According to [19]: b.p. 76.2-76.4° (103 mm), n_D^{20} 1.4185.

4, 4-Dimethyloctene-1. Not described in the literature. Yield 10.5%; b.p. 144° (742 mm), n_D^{20} 1.4227, d_4^{20} 0.7447, MR_D 47.93; calc. 47.91.

Found %: C 85.59, 85.56; H 14.41, 14.48. $C_{10}H_{20}$. Calculated %: C 85.62; H 14.38.

Hydrogenated over Ni to 4, 4-dimethyloctane. Not described in the literature. Yield 90%; b.p. 155° (753 mm); freezing point below –110°, n_D^{20} 1.4140, d_4^{20} 0.7347, MR_D 48.36; calc. 48.38.

Found %: C 84.38, 84.36; H 15.62, 15.68. $C_{10}H_{22}$. Calculated %: C 84.40; H 15.60.

Raman spectrum λ (cm^{-1}): 286 (2); 300 (4); 333 (1); 358 (2); 483 (3); 472 (0); 499 (3); 541 (1); 733 (3); 757 (5); 786 (1); 878 (4 broad); 896 (4); 936 (4); 1042 (5); 1061 (2); 1078 (1); 1105 (5); 1192 (2 broad); 1219 (2); 1269 (3 broad); 1317 (5); 1379 (5); 1440 (10); 1460 (5).

Not described in the literature. Yield 11%; b.p. 130-131° (740 mm), n_D^{20} 1.4150, d_4^{20} 0.7888, MR_D 45.78; calc. 45.41. Found %: ethoxy groups 31.78; 31.82. $C_9H_{20}O$. Calculated %: ethoxy groups 31.24.

2) 2, 4, 4, 5, 5, 7-Hexamethyloctane. Not described in the literature. Yield 5%; b.p. 216-217°; freezing point +2° (cryst.), n_D^{20} 1.4446, d_4^{20} 0.7902, MR_D 66.70; calc. 66.85.

Found %: C 84.60, 84.81; H 15.01, 15.04. $C_{14}H_{30}$. Calculated %: C 84.76; H 15.24.

Raman spectrum λ (cm^{-1}); 697 (4); 823 (2); 936 (2 broad); 960 (4); 1173 (1); 1219 (3); 1236 (2).

SUMMARY

1. It has been shown that isobutenyl Mg halide reacts even with highly branched ketones in the normal way with the formation of the corresponding tertiary alcohols in yields of 50-60%.

2. The condensation of saturated tertiary alkyl fluorides has been carried out for the first time with Grignard reagents prepared from saturated alkyl chlorides, and also by Yavorsky's method with allyl halides. It has been established that the fluorides give hydrocarbon yields which are 3 times greater than those obtained with the chlorides of analogous structure.

3. It has been shown that the yields of hydrocarbons synthesized by the Grignard-Wurtz method are increased by the introduction of a multiple bond into the alkyl halide in the β-position relative to the halogen-carbon bond (i.e. in the case of σ, π-conjugation), and also in the case of σ, σ-conjugation.

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STUDIES IN THE FIELD OF HETEROCYCLIC CHEMISTRY

XXVII. THE SYNTHESIS AND PROPERTIES OF MONOHALOGENO DERIVATIVES OF 9-PHENYLACRIDINE

P. A. Petyunin and M. E. Konshin

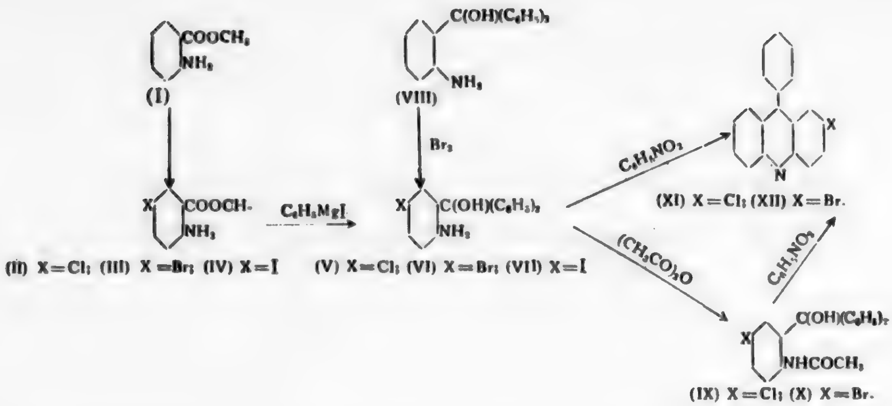
The halogenation of acridine has been insufficiently studied [1]. Since acridine undergoes substitution reactions with difficulty, its halogen derivatives are usually prepared from benzene derivatives containing the required substituent [2]. In this case too, however, it is sometimes necessary to proceed by a more complex route than in the synthesis of the unsubstituted compounds [3-5]. The halogen derivatives of 9-phenylacridine have been studied to an even lesser extent. Thus Dunstan [6, 7], in the chlorination and bromination of 9-phenyl-acridine, isolated a series of halogen derivatives of unknown structure. Lehmstedt [8] prepared the x, x-dibromo-derivative by the action of bromine on 9-phenylacridine. Quite recently Acheson and coworkers [9] studied the bromination of 9-phenylacridine in a medium of carbon tetrachloride; instead of the product of bromination they obtained the addition product – 10-bromo-9-phenylacridinium bromide. These examples constitute all the information we have on the study of the halogen derivatives of 9-phenylacridine.

The present communication is devoted to working out a method for the preparation of monohalogeno derivatives of 9-phenylacridine and to a study of their properties. The synthesis was based on 2-aminotriphenylcarbinol [10]. We attempted unsuccessfully to prepare the starting monohalogeno derivatives of 2-aminotriphenylcarbinol by the direct halogenation of 2-aminotriphenylcarbinol (VIII). For this purpose, (VIII) was treated with bromine in acetic acid or pyridine, and also with N-chloroacetamide in the presence of sodium bromide and sulfuric acid. In all cases a tarry product was obtained which could not be purified by recrystallization from different solvents. The behavior of (VIII) towards halogenating agents is similar to that of triphenylcarbinol, which, as is known, shows a marked inertness to the action of electrophilic reagents [11].

The synthesis of halogeno derivatives of 2-aminotriphenylcarbinol was carried out with good results using organomagnesium compounds. Starting from methyl anthranilate (I), we prepared the 5-chloro- and 5-bromo-derivatives (II, III), using the chloroamide method of M. V. Likhosherstov [12]. The halogenation was carried out using N-chloroacetamide and N, N-dichlorourea; it turned out that N-chloroacetamide gave good results only in the bromination. The chlorination was also carried out using N, N-dichlorourea. The iodo derivative (IV) was obtained by the reaction of (I) with iodine chloride.

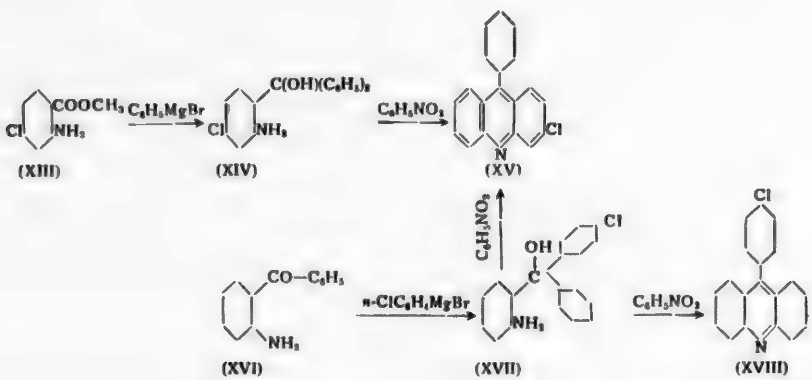
When the halogeno derivatives of methyl anthranilate (II, III, IV) were treated with phenyl magnesium iodide, the corresponding halogeno derivatives of 2-aminotriphenylcarbinol (V, VI, VII) were obtained in good yield. The latter, in contrast to 2-aminotriphenylcarbinol (VIII), are very weak bases and do not dissolve in dilute mineral acids or in concentrated hydrochloric acid. They exhibit the phenomenon of halochromism and give solutions of a deep red color with concentrated sulfuric acid. When (V, VI) are heated with acetic anhydride, they readily form the N-acetyl derivatives (IX, X) which also exhibit the phenomenon of halochromism. When (V, VI) or their acetyl derivatives (IX, X) are heated in nitrobenzene, the 2-halogeno derivatives of 9-phenylacridine are formed (XI, XII).

The acridine ring closes more readily in the halogeno substituted 2-aminotriphenylcarbinols than in their N-acetyl derivatives. Thus when the experiments were carried out with the latter (IX, X), a longer time of heating was required and the reaction products were obtained in lower yield.



The method worked out by us for the preparation of halogeno substituted 2-aminotriphenylcarbinols is not applicable to the iodo derivative, since in this case very marked dehalogenation is observed. The experiments were carried out with (VII) in a medium of nitrobenzene or amyl alcohol.

The action of phenyl magnesium bromide on methyl 4-chloroanthranilate (XIII) led to the formation of 4-chloro-2-aminotriphenylcarbinol (XIV), which gave 3-chloro-9-phenylacridine (XV) when heated in nitrobenzene. The reaction of p-chlorophenyl magnesium bromide with 2-aminobenzophenone (XVI) gave 4'-chloro-2-aminotriphenylcarbinol (XVII). The closure of the acridine ring in the latter may take place in two directions with the formation of a mixture of isomers (XV, XVIII). We were able to separate only one of the possible isomers (XV) in 26.8% yield.



EXPERIMENTAL

Methyl 5-chloroanthranilate (II). 2 ml concentrated sulfuric acid was added to a solution of 30.2 g (0.2 mole) of (I) in 100 ml 80% acetic acid. 12.9 g (0.1 mole) of N, N-dichlorourea was added with stirring (temperature below 25-30°). When the reaction was complete (test with starch paper) the reaction mass was poured into 500 ml water and the reaction product extracted with ether. The solvent was removed and the substance distilled at 150-153° (10 mm). Yield 25 g (67.4%). Plates (from methyl alcohol) with m.p. 69° [13].

Methyl 5 bromoanthranilate (III). 18.1 g (0.12 mole) of (I) was dissolved in 50 ml of 80% acetic acid, and 3 ml concentrated sulfuric acid added, followed by 16.7 g (0.12 mole) of sodium bromide dissolved in a small quantity of water. The bromination was carried out using 11.8 g N-chloroacetamide. Yield 15 g (54.4%). Needles (from methyl alcohol) with m.p. 74° [14].

Methyl 5-iodoanthranilate (IV). A solution of 16.2 g iodine chloride in 30 ml 80% acetic acid was added to a solution of 15.1 g of (I) in 50 ml 80% acetic acid. The reaction mass was maintained at 25-30° for 30 minutes and then diluted with three times its volume of water. The precipitate which separated was treated in the usual way. Crystals (from alcohol) with m.p. 83-85°. Yield 12.5 g (48.7%).

Found %: N 5.31, 5.33. $C_8H_8O_2NI$. Calculated %: N 5.05.

5-Chloro-2-aminotriphenylcarbinol (V). A solution of 14.8 g (0.08 mole) of (II) in 50 ml ether was added to phenyl magnesium iodide prepared from 65.3 g (0.32 mole) iodobenzene and 7.8 g magnesium in 150 ml ether. To complete the reaction the contents of the flask were heated for 1 hour, after which the organomagnesium complex was broken up with dilute acetic acid. The ether layer was removed and treated with steam. The residue was crystallized from alcohol. Soluble in the common organic solvents, insoluble in dilute mineral acids and in concentrated hydrochloric acid. The solutions in concentrated sulfuric acid have a deep red color. Yield 16.5 g (66.6%). Plates with m.p. 123.5-125°.

Found %: N 4.34, 4.40; Cl 11.51, 11.20. $C_{19}H_{16}ONCl$. Calculated %: N 4.52; Cl 11.46.

The picrate was obtained by mixing alcoholic solutions of the substance and picric acid. Yellow crystals (from alcohol) with m.p. 130° (with decomp.).

N-Acetyl-5-chloro-2-aminotriphenylcarbinol (IX). Obtained by heating 4 g of (V) and 8 ml acetic anhydride for 1 hour. Readily soluble in acetic acid and benzole, soluble with difficulty in alcohol and benzene. Soluble in concentrated sulfuric acid with the production of a deep red color. Yield 3.4 g (74.9%). Prisms (from alcohol) with m.p. 158.5-159.5°.

Found %: N 3.67, 3.88 $C_{21}H_{18}O_2NCl$. Calculated %: N 3.98.

5-Bromo-2-aminotriphenylcarbinol (VI). Starting materials: 14.95 g (0.065 mole) of (III), 53 g (0.26 mole) iodobenzene and 6.26 g magnesium. Soluble in the common organic solvents, insoluble in dilute mineral acids and concentrated hydrochloric acid. Soluble in concentrated sulfuric acid with the production of a deep red color. Yield 19.3 g (83.9%). Rods (from alcohol) with m.p. 138-139.5°.

Found %: N 3.61, 3.68; Br 22.58, 22.54. $C_{19}H_{16}ONBr$. Calculated %: N 3.96; Br 22.58.

Picrate, m.p. approximately 130° (with decomp.).

N-Acetyl-5-bromo-2-aminotriphenylcarbinol (X). Obtained in 84.9% yield. Readily soluble in alcohol and acetic acid. The solutions in concentrated sulfuric acid have a deep red color. Prisms (from alcohol) with m.p. 176-177°.

Found %: N 3.20, 3.29. $C_{21}H_{18}O_2NBr$. Calculated %: N 3.53.

5-Iodo-2-aminotriphenylcarbinol (VII). The reaction was carried out with 5.54 g (0.02 mole) of (IV) and phenyl magnesium bromide prepared from 12.56 g (0.08 mole) bromobenzene and 1.92 g (0.08 mole) magnesium in 50 ml ether. Soluble in alcohol, ether, benzene and acetic acid. Gives a deep red color with concentrated sulfuric acid. Yield 6.9 g (86.2%).

Plates (from alcohol) with m.p. 149° (with decomp.).

Found %: N 3.55, 3.19. $C_{19}H_{16}ONI$. Calculated %: N 3.49.

2-Chloro-9-phenylacridine (XI). Obtained by boiling 4 g of (V) in 4 ml nitrobenzene for 15 minutes (yield 2.7 g, 72%) or by heating 1 g of (IX) in 2 ml nitrobenzene for 2 hours on a sand bath (yield 0.35 g, 42.6%). In contrast to the method described earlier [10], the reaction mass was not acidified with hydrochloric acid before the treatment with steam, and after removal of the nitrobenzene the acridine base was recrystallized from a suitable solvent. In the experiments carried out with the N-acetyl derivatives (IX, X), the acridine bases were extracted from the tarry residue, after removal of the nitrobenzene, with 10% hydrochloric acid, and then treated as in [10]. Readily soluble in acetic acid and alcohol. Soluble in dilute hydrochloric acid with a weak

yellow-green fluorescence. Light yellow needles (from alcohol) with m.p. 150-151.5°.

Found %: N 4.78, 4.56; Cl 12.10, 11.98. $C_{19}H_{12}NCl$. Calculated %: N 4.73; Cl 12.25.

The picrate was obtained by mixing alcoholic solutions of the substance and picric acid. Bright yellow needles (from alcohol) with m.p. 219-220°.

2-Bromo-9-phenylacridine (XIII). Prepared by heating 1 g of (VI) in 1 ml nitrobenzene for 10 minutes (yield 0.5 g, 53%) and also by heating 1.5 g (X) in 2 ml nitrobenzene for 2 hours on a sand bath (yield 0.63 g, 49.8%). Soluble in alcohol and acetic acid. The solutions in dilute hydrochloric acid exhibit a weak yellow-green fluorescence. Light yellow needles (from alcohol) with m.p. 145-146°.

Found %: N 4.32, 4.49; Br 23.71, 23.75. $C_{19}H_{12}NBr$. Calculated %: N 4.19; Br 23.93.

Picrate, yellow needles (from alcohol) with m.p. 234-235°.

4-Chloro-2-aminotriphenylcarbinol (XIV). Starting materials: 3.7 g of (XIII),* 12.5 g bromobenzene and 1.96 g magnesium in 30 ml ether. Soluble in alcohol, ether, benzene and acetic acid. Gives an orange coloration with concentrated sulfuric acid. Hexahedral prisms (from alcohol) with m.p. 138-139°.

Found %: N 4.28, 4.26. $C_{19}H_{16}ONCl$. Calculated %: N 4.52.

3-Chloro-9-phenylacridine (XV). Prepared by heating 2 g of (XIV) in 2 ml nitrobenzene for 15 minutes (yield 1 g, 53.4%), or from 1 g of (XVII) in 1 ml nitrobenzene (yield 0.25 g, 26.8%). Soluble in alcohol, benzene and acetic acid. The solutions in mineral acids exhibit a weak yellow-green fluorescence. Yellow needles (from alcohol) with m.p. 151.5-152°.

Found %: N 4.67, 4.79. $C_{19}H_{12}NCl$. Calculated %: N 4.73.

Picrate, yellow crystals (from alcohol) with m.p. 251-252°.

4'-Chloro-2-aminotriphenylcarbinol (XVII). The reaction was carried out with 4.9 g of (XVI) and p-chlorophenyl magnesium bromide prepared from 14.4 g p-bromochlorobenzene and 1.8 g magnesium in 50 ml ether. Soluble in alcohol, benzene and acetic acid; insoluble in dilute mineral acids. Gives a deep red coloration with concentrated sulfuric acid. Yield 5.9 g (76.5%). Needles (from alcohol) with m.p. 97°.

Found %: N 4.20, 4.51. $C_{19}H_{16}ONCl$. Calculated %: N 4.52.

SUMMARY

1. A method has been worked out for the preparation of monohalogeno derivatives of 9-phenylacridine, based on halogeno substituted 2-aminotriphenylcarbinols and their N-acetyl derivatives.

2. It has been established that closure of the acridine ring takes place more readily in the halogeno substituted 2-aminotriphenylcarbinols than in their acetyl derivatives.

3. From the example of 5-iodo-2-aminotriphenylcarbinol, it has been shown that the method cannot be recommended for the synthesis of iodo derivatives of 9-phenylacridine, since marked dehalogenation takes place.

4. The chloroamide method has been used with good results for the halogenation of methyl anthranilate; it has also been established that N-chloroacetamide gives good results in the bromination of methyl anthranilate, but not in the chlorination. The chlorinationof this substance proceeds smoothly when N, N-dichlorourea is used.

5. A number of halogeno derivatives of 2-aminotriphenylcarbinol, which are not described in the literature, have been prepared by the action of phenyl magnesium bromide on halogeno derivatives of methyl anthranilate, and the properties of these compounds have been studied.

6. A number of monohalogeno derivatives of 9-phenylacridine, which are not described in the literature, have been prepared and their properties have been studied.

* Prepared by the esterification of 4-chloroanthranilic acid; m.p. 68-69° [15].

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REACTIONS OF MAGNESYLAMINES

II. A NEW REACTION OF ALDEHYDES

P. A. Petyunin and L. A. Tetyueva

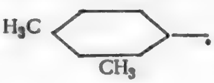
One of us and coworkers [1] were the first to study the reaction of N, N-bis-(halogenomagnesium)-arylamines with acid halides and esters; in this work preparative methods were worked out for obtaining arylamides of carboxylic acids and diacyl derivatives of aromatic amines. In the present work a description is given of the results of a study of the reaction between N, N-bis-(halogenomagnesium)-arylamines and benzaldehyde. On the basis of the results of the previous communication it might have been supposed that the magnesylamines mentioned would react with aldehydes in the same way as with the free amine, i.e. with the formation of Schiff's bases. The experiments, however, did not confirm this hypothesis. The reaction leads to the formation of N-arylamides of benzoic acid and in the general form may be represented by the following scheme:

$$2C_6H_5CHO + C_6H_5N(MgBr)_2 \longrightarrow C_6H_5C(OMgBr) = NC_6H_5 +$$
$$+ C_6H_5CH_2OMgBr \xrightarrow{H_2O} C_6H_5CONHC_6H_5 + C_6H_5CH_2O$$

Under the influence of the N, N-bis(halogenomagnesium)-arylamine, two molecules of benzaldehyde are converted into benzyl alcohol and the arylamide of benzoic acid. It is true that the alcohol has not as yet been isolated by us, but the possibility of its formation cannot be doubted.

The reaction studied by us recalls the well-known Cannizzaro-Tishchenko oxidation-reduction reaction, and differs from it in the structure of one of the end products. It should be noted that there are no reports of this reaction in the literature, and it has evidently been studied by us for the first time. We have carried out the reaction between benzaldehyde and $ArN(MgBr)_2$, where:

$Ar = C_6H_5-$, $o\text{-}CH_3C_6H_4-$, $m\text{-}CH_3C_6H_4-$, $p\text{-}CH_3C_6H_4-$, $p\text{-}ClC_6H_4-$, $p\text{-}BrC_6H_4-$,

$p\text{-}CH_3OC_6H_4-$, $p\text{-}C_2H_5OC_6H_4-$, $\alpha\text{-}C_{10}H_7-$, $\beta\text{-}C_{10}H_7-$ and .

EXPERIMENTAL

Working method (the experiments were carried out in the usual apparatus used for Grignard syntheses). A solution of 0.05 mole of the aromatic amine in 20 ml ether was added to a solution of ethyl magnesium bromide, prepared in the usual way from 0.1 mole ethyl bromide and 0.1 mole magnesium in 30 ml ether. The reaction mass was then heated for 10 minutes on the water bath, so that both hydrogen atoms of the amino group reacted. A solution of 0.1 mole of freshly distilled benzaldehyde in 15 ml ether was added to the solution obtained; during this operation vigorous boiling of the ether was observed. The organomagnesium complex was broken up with 10% hydrochloric acid, the ether layer removed and treated with steam. To accelerate the removal of the unreacted benzaldehyde, the distillation was carried out as in the method of [2]. The reaction product was left in the distillation flask and was then recrystallized from a suitable solvent. The experimental results, together with the analysis data for the compounds obtained, are given in Table 1, from which it can be seen that the yield of arylamines depends on the nature of the aromatic dimagnesylamine and amounts to 4.4-21.2%, calculated from the amine taken for the reaction. Since the benzarylamides were obtained in low yield, a study was made, taking the reaction between benzaldehyde and N, N-bis-(bromomagnesium)-aniline as an example, of the influence of time of heating (Table 2) and of the ratio of reagents (Table 3) on the yield of benzanilide.

TABLE 1

Dimagnesylamine	Reaction product	Yield (%)	Melting point		Analysis for nitrogen (%)		Molecular weight determination, by the Rast method	
			our data	literature data [3]	found	calc.	M found	M calc.
$C_6H_5N(MgBr)_2$	$C_6H_5CONHC_6H_5$	17.3	161—162°	162°	7.36	7.1	188.1	197.1
m-$CH_3C_6H_4N(MgBr)_2$	$C_6H_5CONHC_6H_4CH_3$-m	11.4	123—124	125	6.40. 6.45	6.63	204	211
p-$CH_3C_6H_4N(MgBr)_2$	$C_6H_5CONHC_6H_4CH_3$-p	17.1	157—158	157	6.58. 6.50	6.63	203	211
p-$ClC_6H_4N(MgBr)_2$	$C_6H_5CONHC_6H_4Cl$-p	12.9	190.5	192—193	6.07. 5.98	6.08	224	231.4
p-$BrC_6H_4N(MgBr)_2$	$C_6H_5CONHC_6H_4Br$-p	12.6	202	202	4.95. 4.93	5.07	266	275.9
p-$CH_3OC_6H_4N(MgBr)_2$	$C_6H_5CONHC_6H_4OCH_3$-p	8.82	155—156	156	6.36. 6.34	6.12	—	—
p-$C_2H_5OC_6H_4N(MgBr)_2$	$C_6H_5CONHC_6H_4OC_2H_5$-p	11.6	172—173	173	6.05. 6.00	5.81	237	241
α-$C_{10}H_7N(MgBr)_2$	$C_6H_5CONHC_{10}H_7$-α	21.2	160—162	162	5.42. 5.70	5.67	235	247
β-$C_{10}H_7N(MgBr)_2$	$C_6H_5CONHC_{10}H_7$-β	20.1	159—161	161	5.84. 5.78	5.67	236	247
o-$CH_3C_6H_4N(MgBr)_2$	$C_6H_5CONHC_6H_4CH_3$-o	14.3	142—143.5	143	6.40. 6.45	6.63	203.8	211
H_3C-$C_6H_3(CH_3)$-$N(MgBr)_2$	C_6H_5CONH-$C_6H_3(CH_3)$-CH_3	4.4	190	192	6.22. 6.18	6.22	214	225

TABLE 2

Exp. No.	Time of heat-ing (in hrs)	Yield of $C_6H_5NHCOC_6H_5$	
		(r)	(%)
1	without heating	1.6	16.26
2	1	1.7	17.25
3	2	1.6	16.26
4	2.5	1.7	17.25
5	10	1.7	17.25

Note. The experiments were carried out with 0.1 mole benzaldehyde and 0.05 mole N, N-bis-(bromomagnesium)-aniline. The reaction product was isolated as in the previous experiments.

TABLE 3

Exp. No.	$C_6H_5(Mg)Br_2$ (in moles)	C_6H_5CHO (in moles)	Yield of $C_6H_5NHCOC_6H_5$	
			(r)	(%)
1	0.05	0.05	0.1	1.01
2	0.05	0.1	1.6	16.26
3	0.05	0.15	1.6	16.26

Note. In all the experiments the time of heating was 2 hours.

It can be seen from the data given in Table 2 that the time of heating the reaction mass has practically no influence on the yield of benzanilide. In experiment 1 the reaction was carried out without heating and the reaction product was obtained in a pure state, whereas with heating for 10 hours (experiment 5), a considerable amount of tar formation was observed, although the substance was this time obtained in slightly higher yield. The relative proportions of the reacting materials has a marked influence on the yield of benzaldehyde. Thus when N, N-bis-(bromomagnesium)-aniline is added to benzaldehyde in the ratio 1 : 1 (experiment 1), the reaction takes place vigorously, but when the reaction mass is broken up the benzaldehyde is almost quantitatively recovered. The greatest yield of benzaldehyde is obtained in the case where 2 moles of benzaldehyde are taken for 1 mole dimagnesylaniline (experiment 2). The yield remains unchanged, even if the amount of benzaldehyde is increased to 3 moles (experiment 3),

SUMMARY

1. The reaction between benzaldehyde and N, N-bis-(halogenomagnesium)-arylamines has been studied for the first time; it has been established that the final reaction products are the corresponding N-arylamides of benzoic acid.

2. From the nature of the final products, the reaction studied by us may be classified as belonging to the oxidation-reduction type of reaction.

3. A study has been made, taking the reaction between benzaldehyde and N, N-bis-(bromomagnesium)-aniline as an example of the influence of the time of heating and of the ratio of the reacting materials on the yield of benzanilide.

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METHOD FOR SYNTHESIZING ARYLTHIOUREAS AND THE CORRESPONDING MUSTARD OILS

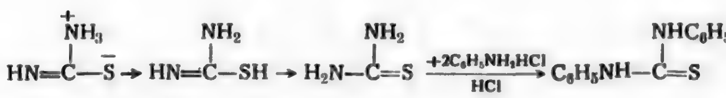
N. I. Volynkin

Symmetrical alkyl or aryl derivatives of thiourea are usually prepared by the reaction of carbon disulfide with the corresponding amines [1-3] or by the reaction of amines with mustard oils [4]. The derivatives of urea can be prepared directly from urea and an amine, for example, phenylurea or carbanilide [5, 6]; the possibility of preparing diaryl- and dialkylthioureas from thiourea and amines is not described in the literature.

When the chemical properties of urea and thiourea are compared, it is seen that as well as certain common reactions, there exist a number of characteristic properties which are shown only by urea or by thiourea. Urea is known in only one form; its ethers are obtained only in the iso form, starting from cyanamide hydrochloride or from the reaction of dimethyl sulfate on urea in the presence of alkali. The preparation of O-alkyl derivatives of urea in alkaline solution indicates the possibility of the existence of urea in the form of isourea at pH greater than 7. In neutral and acid medium urea reacts in the normal form.

Most of the reactions of thiourea, on the contrary, correspond to the structure of isothiourea, i.e. tautomeric equilibrium exists between thiourea and isothiourea. When thiourea is treated with an alkyl halide, the isothiourea derivative is obtained. The oxidation of thiourea with potassium permanganate or ferric chloride in the presence of acid leads to the formation of the disulfide, which also confirms that thiourea exists for the most part in the iso form. Werner considers [7] that in neutral aqueous solutions thiourea exists as the inner salt of the iso form. In this way a short examination of the chief chemical properties of urea and thiourea shows that certain of their reactions are not analogous.

In a study of the synthesis of p-ethoxyphenylurea by the reaction of p-phenetidine with urea, which was carried out in the first stage of the present work, the influence of the pH of the medium on the course of the reaction was established; for example, when the above mixture was boiled under reflux for 6 hours, no dulcin was formed at pH 8, but at pH ≤ 6 the reaction was complete in a few minutes with a yield of more than 70% phenetolecarbamide. A direct attempt to apply the results of the study of the synthesis of phenetolecarbamide to the preparation of arylthioureas gave no positive results. When aqueous solutions of thiourea and aniline hydrochloride were boiled for several hours (100-102°) at pH 6, no diphenylthiourea was formed, which may be explained by the immobility of the hydrogens of the amide and imide groups of isothiourea, if this is regarded as an inner salt; isourea gives no inner salt. In the absence of water and at high temperature the reaction took place with the formation of diphenylthiourea in 69-81% yield.



At the same time decomposition of the thiourea took place under the influence of the high temperature, with the liberation of NH_3, CS_2, H_2S. Repeated experiments showed that the yield and rate of the reaction are increased if the ammonia evolved is combined by the gradual addition of an equivalent amount of 30% hydrochloric acid.

Reduction of the pH value below 6 made it possible to prepare phenyl mustard oil, which is formed from the diphenylurea. The formation of the mustard oil with increased acidity was accelerated at the same time by raising the temperature above 125°. When a mixture of thiourea, water and aniline hydrochloride was heated at 100-102° for several hours in the presence of mineral acid, as in the case described above, no diphenylthiourea or phenyl mustard oil was formed.

The preparation of mustard oils from the corresponding symmetrical diarylthioureas by heating with mineral acids has been studied by a number of investigators [8, 9], and for good yields it has been necessary to use an excess of mineral acid. When thiourea is heated with mineral acids, however, this should lead to its decomposition, as a result of which a good yield of phenyl mustard oil cannot be obtained in this way. Test experiments confirmed this hypothesis; the maximum yield of mustard oils at 125-180° and pH below 6 proved to be lower than 20%.

Further experiments on the synthesis of phenyl mustard oil were carried out in two ways: first–by the condensation of thiourea with aniline hydrochloride at pH 6-6.5 and temperatures up to 180°, and second–by the addition of mineral acid to the reaction mixture with subsequent distillation of the phenyl mustard oil with water at a lower temperature. The yield of phenyl mustard oil in these conditions rose to 70%. The use of other amines in place of aniline led to the formation of the corresponding symmetrical arylthioureas and mustard oils.

EXPERIMENTAL

The experiments were carried out in round-bottomed flasks and Wurtz flasks, of 100 and 1000 ml capacity, fitted with reflux condenser and thermometer lowered into the reaction mixture. The hydrogen ion concentration was determined colorimetrically using the indicators methyl orange, congo red, methyl red, nitrophenol, dibromothymolphthalein, rosolic acid, thymolphthalein, and also by means of special papers for the determination of pH with an accuracy of 0.2-0.5.

1. The preparation of p-ethoxyphenylurea (dulcin). 100 g p-phenetidine, 200 g urea and 600 ml water at pH 8 were boiled under reflux for 8 hours. The mixture was cooled and 4.5 g of dulcin isolated by crystallization. Yield 3.2%. When the same mixture was boiled at pH 7, 40 g of dulcin was obtained (yield 26%). Finally, when the experiment was repeated at pH 6,112 g of dulcin with m.p. 171° was obtained (yield 71%).

2. The preparation of diphenylthiourea. 80 g thiourea, 190 g aniline and approximately 230 g 29% hydrochloric acid (technical) to an orange color with congo red were placed in a liter flask. The mixture was heated to the boil to remove the water. When the temperature rose from 120 to 180°, phenyl mustard oil was found in the distillate together with the water. At the end of the reaction the contents of the flask solidified and colorless crystals sublimed. The flask was cooled to 80°, boiling water added and the mixture poured into a liter beaker. The cooled mass was broken up and washed with water to remove the water-soluble materials (ammonium salts, aniline hydrochloride, etc.), after which the crude diphenylthiourea was filtered off, dried at 40-50° and recrystallized from alcohol. 140 g (55.5%) of material with m.p. 154° was obtained. In the preparation of the phenyl mustard oil, recrystallization from alcohol proved impossible.

3. The preparation of phenyl mustard oil. 80 g thiourea, 140 g aniline and 180 g 30% hydrochloric acid were placed in a liter flask and the mixture boiled to remove the water. When the temperature was raised above 140°, crystals of diphenylthiourea were seen to be subliming and when this took place 50 ml of 20% hydrochloric acid was added. The phenyl mustard oil began to distill over with the water. When new crystals of diphenylthiourea appeared, a further 50 ml of hydrochloric acid 20% was added and this was continued until all the oil had distilled.* The oil was separated and distilled and the fraction boiling at 219-220° was collected. The phenyl mustard oil solidified at –22.5°, d_4^{25} 1.128. Yield 60-80 g (57.1%).

4. The preparation of 2-methylphenylene isothiocyanate and 3-methylphenylene isothiocyanate. When the aniline of experiment 3 was replaced by o-toluidine, 45 g (25%) of 2-methylphenylene isothiocyanate with b.p. 238.5° was obtained, and when m-toluidine was used as the amine, 60 g (42%) of 3-methylphenylene isothiocyanate with b.p. 243° was obtained.

* The acid may be added all at once, but in this case it is necessary to heat to 180°, and then, after cooling to 120°, to add the total amount of acid (200 ml).

SUMMARY

1. The optimum conditions for the condensation of urea with amines, for example, with phenetidine, have been established with the aim of preparing phenetolecarbamide.

2. It is apparent that the condensation of thiourea and an amine does not take place in the conditions which are favorable for the condensation of urea.

3. When the temperature is raised above 120° at pH approximately 6, the condensation of thiourea and an amine takes place with the formation of symmetrical arylthioureas in good yield.

4. The condensation of thiourea and an amine at pH 6 leads to the direct synthesis of a mustard oil.

5. Methods have been worked out for the synthesis of certain arylthioureas and the corresponding mustard oils from thiourea and arylamines.

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DINITROBENZENESULFONIC ACIDS AND THEIR ESTERS

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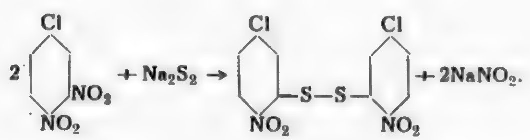
In connection with a study of the rate of formation of quaternary salts by the action of nitrobenzenesulfonates on heterocyclic bases [1] we found it necessary to prepare the esters of a number of nitro- and dinitrobenzenesulfonic acids. It turned out that only the esters of mononitrobenzenesulfonic acids are known; no single ester of dinitrobenzenesulfonic acid has been described. Only two of the dinitrobenzenesulfonic acids themselves have been prepared, namely the 2, 4- and the 3, 5-acids.

In the present communication a description is given of the synthesis of 2, 3-, 2, 5- and 3, 4-dinitrobenzenesulfonic acids, their esters and other derivatives, and also of several new esters of known nitro- and dinitrobenzenesulfonic acid.

o- and p-Nitrobenzenesulfonic acids are prepared by the action of sodium disulfide on o- and p-nitrochlorobenzene and oxidation of the disulfides obtained [2]. This method cannot be used with 2, 3-, 2, 5- and 3, 4-dinitrochlorobenzenes, since in these compounds the nitro group is more labile than the chlorine atom in nucleophilic substitution reactions [3]. With 3, 4-dinitrochlorobenzene, for example, sodium disulfide reacts according to the equation [4]:



For the same reason the exchange reaction with sodium sulfite cannot be used. The essential difficulty in the synthesis of the above dinitrobenzenesulfonic acids is their low stability. Even the evaporation of their aqueous solutions on the water bath may lead to gradual decomposition with the evolution of oxides of nitrogen.

Taking these factors into account, we have worked out the following method for the synthesis of 2, 3-, 2, 5- and 3, 4-dinitrobenzenesulfonic acids. Three dinitroacetanilides: the 2, 3-, 2, 5- and 3, 4-dinitro isomers, were prepared by nitrating m-nitroacetanilide, isolated and hydrolyzed with concentrated sulfuric acid at 110° (not more than 5 minutes for 2, 3-dinitroacetanilide!) to give the three isomeric dinitroanilines [3, 6]. Each of these was diazotized, the diazo solution treated with sodium xanthate in an acid medium* below 0°, the diazoxanthate decomposed at 60-70° with the evolution of nitrogen and the formation of the aryl xanthate and the latter oxidized with nitric acid to the corresponding sulfonic acid:

$$(NO_2)_2C_6H_3NH_2 \longrightarrow (NO_2)_2C_6H_3N_2SO_4H \quad (NO_2)_2C_6H_3N_2SC(S)OC_2H_5 \longrightarrow$$
$$\longrightarrow (NO_2)_2C_6H_3SC(S)OC_2H_5 \longrightarrow (NO_2)_2C_6H_3SO_3H.$$

* The solution should not be neutralized with sodium acetate, since this precipitates the diazo hydrates.

Table 1 shows a number of derivatives of the three new dinitrobenzenesulfonic acids, prepared for the identification of the latter, together with their melting points and analysis data.

TABLE 1

Formula	Melting point	Nitrogen content (%) found	Nitrogen content (%) calculated
2,3-$(NO_2)_2C_6H_3SO_3K$ . . .	—	9.61, 9.80	9.78
2,5-$(NO)_2C_6H_3SO_3K$	—	9.66, 9.76	9.78
		% S: 11.02, 11.24	% S: 11.18
2,5-$(NO_2)_2C_6H_3SO_2Cl$ . . .	83—84°	10.55, 10.58	10.51
2,5-$(NO_2)_2C_6H_3SO_2NH_2$ . .	197	16.84, 16.77	17.00
2,5-$(NO_2)_2C_6H_3SO_2NHC_6H_5$	155	12.84, 12.81	13.00
3,4-$(NO_2)_2C_6H_3SO_3K$ . . .	—	9.60, 9.54	9.78
3,4-$(NO_2)_2C_6H_3SO_2Cl$ . . .	59	10.56, 10.37	10.51
3,4-$(NO_2)_2C_6H_3SO_2NH_2$ . .	165—166	16.64, 16.73	17.00

With L. M. Yagupolsky, we have also prepared the hitherto unknown 2-nitro-4-trifluoromethylbenzenesulfonic acid. This was synthesized according to the following scheme:

$$2,4\text{-}(NO_2)(CF_3)C_6H_3Cl \xrightarrow{Na_2S_2} [2,4\text{-}(NO_2)(CF_3)C_6H_3S-]_2 \xrightarrow{HNO_3} 2,4\text{-}(NO_2)(CF_3)C_6H_3SO_3H.$$

The esters of the nitrobenzenesulfonic acids were prepared in the usual way by the action of alkoxides on the sulfonyl chlorides [7]. A number of precautions must be observed when this method is used for the synthesis of esters of the dinitrobenzenesulfonic acids. Under the influence of alkaline reagents, the dinitrobenzenesulfonic acids may split off the sulfonate group (2,4-dinitrobenzenesulfonic acid) or a nitro group (2,3-, 2,5- and 3,4-dinitrobenzenesulfonic acids). The reaction with the dinitrobenzenesulfonyl chlorides should therefore be carried out at a temperature of approximately $-5°$, while an amount of alkoxide exactly equivalent to the sulfonyl chloride should be added to the chloride solution, and not vice versa.

Occasionally the esters of the dinitrobenzenesulfonic acids are not obtained even when these conditions are observed. Thus, for example, in the reaction between 2,4-dinitrobenzenesulfonyl chloride and monosodium glycol we were able to isolate only the dinitrophenyl glycol ether, according to the equation:

$$2,4\text{-}(NO_2)_2C_6H_3SO_2Cl + NaOCH_2CH_2OH \longrightarrow 2,4\text{-}(NO_2)_2C_6H_3OCH_2CH_2OH^* + NaCl + SO_2.$$

In an attempt to prepare the corresponding methyl ester from 2,5-dinitrobenzenesulfonyl chloride, a mixture of products was obtained from which the only compound which could be isolated was methyl 2-hydroxy-5-nitrobenzenesulfonate.

The most reliable method for the preparation of the esters of dinitrobenzenesulfonic acids is the reaction of their silver salts with alkyl iodides. The methyl esters of 2,3- and 2,5-dinitrobenzenesulfonic acids were prepared in this way.

The hitherto unknown esters of nitro- and dinitrobenzenesulfonic acids are given with their melting points and analysis data in Table 2.

The esters of o-nitrobenzenesulfonic acid prepared by us by the action of the alkoxides of the alcohols from n-propyl to n-octyl alcohol on o-nitrobenzenesulfonyl chloride did not crystallize and could not be distilled without decomposition of the oil.

* The compound was identified by taking a mixed melting point with a specimen prepared by an alternative method [8].

TABLE 2

Formula	Melting point	Nitrogen content (%)	
		found	calculated
$2,3-(NO_2)_2C_6H_3SO_3CH_3$ . . .	153°	10.57, 10.48	10.69
$2,4-(NO_2)_2C_6H_3SO_3CH_3$ . . .	86.5	10.71, 10.74	10.69
$2,4-(NO_2)_2C_6H_3SO_3C_2H_5$ . . .	97	10.11, 10.23	10.14
$2,4-(NO_2)_2C_6H_3SO_3C_6H_5$ . . .	115—116	8.42, 8.58	8.64
$2,4-(NO_2)_2C_6H_3SO_3C_6H_4NO_2$-o	139	11.46, 11.32	11.38
$2,5-(NO_2)_2C_6H_3SO_3CH_3$ . . .	86—87	10.65, 10.70	10.69
$3,4-(NO_2)_2C_6H_3SO_3CH_3$ . . .	91—92	10.53, 10.57	10.69
$3,5-(NO_2)_2C_6H_3SO_3CH_3$ . . .	162	10.59, 10.64	10.69
$3,5-(NO_2)_2C_6H_3SO_3C_6H_{11}$ . . .	82—83	8.55, 8.57	8.49
$2,4-(NO_2)(CF_3)C_6H_3SO_3CH_3$.	86—87	% S: 11.70, 11.78	11.80
$2,4-(NO_2)ClC_6H_3SO_3CH_3$ . .	101—102	5.58, 5.70	5.57
$2,4-(NO_2)ClC_6H_3SO_3C_2H_5$ . .	97.5	—	—
$2,4-(NO_2)ClC_6H_3SO_3C_3H_7$-н. .	63	% S: 12.71, 12.87	12.70
$2,4-(NO_2)ClC_6H_3SO_3C_3H_7$-изо	59—60	—	—
$(o-NO_2C_6H_4SO_3CH_2)_2$	110	6.37, 6.30	6.28
$p-NO_2C_6H_4SO_3C_8H_{17}$-н. . . .	73	9.69, 9.84	10.15
$p-NO_2C_6H_4SO_3C_6H_{11}$	78(decomp)	4.90, 4.85	4.91

EXPERIMENTAL

2, 5-Dinitrobenzenesulfonic acid. 20.59 g 2, 5-dinitroaniline was dissolved in 75 ml concentrated sulfuric acid. The solution was cooled to 0° and 8.25 g of finely powdered sodium nitrite added gradually with mechanical stirring. The mixture was then heated gradually to 60° and kept at this temperature for 30 minutes. The solution of the diazo compound was poured on to 400 g of ice, and a solution of 31.2 g sodium xanthate in 150 ml water added slowly with stirring at —5° to the solution obtained. The mixture was stirred at —5° for a further 30 minutes. The voluminous yellow diazoxanthate precipitate obtained was quickly filtered off, washed with ice water and then decomposed by adding to a large vessel fitted with a stirrer and containing 100 ml water, heated to 60-70°. The decomposition took approximately 40 minutes; towards the end of the reaction the solution was raised to the boil. The oil which separated was extracted with 800 ml ether, the ether distilled off and the residue in the flask acidified with 100 ml nitric acid (d 1.5). The acid was added dropwise, after which the mixture was heated for 2 hours on a boiling water bath; during this time part of the nitric acid distilled off and approximately 60 ml of liquid remained in the flask. The sulfonic acid which precipitated on cooling in the form of white needles, was filtered off on a glass filter, pressed out and washed with benzene and ether. Yield 14.5 g (58%), m.p. 174-176°. The sulfonic acid is readily soluble in water, alcohol and acetone, almost insoluble in benzene, chloroform and ether. When an aqueous solution of the acid was neutralized with the calculated quantity of potassium carbonate, the potassium salt was obtained as pale yellow needles.

The chloride was prepared by the action of 26 g phosphorus pentachloride on 6.2 g of the acid. The mixture gradually became hot and a vigorous evolution of hydrogen chloride was observed. When the reaction had slowed down, the flask was heated for a further hour at 120°, after which the phosphorus oxychloride was distilled off. The cooled mixture was poured on to 150 g ice. The material which solidified was filtered off, washed with water and dried. After two recrystallizations from benzene, 2.83 g (43%) of the sulfonyl chloride with m.p. 83-84° was obtained.

The amide was prepared by the action of an aqueous solution of ammonia on an ethereal solution of the sulfonyl chloride. The ether was removed, the ammoniacal solution filtered, and the amide in solution in the ammonia was precipitated with hydrochloric acid and recrystallized from alcohol. Light yellow needles with m.p. 197°.

The anilide was prepared by the action of an equimolecular amount of aniline on an ethereal solution of the sulfonyl chloride. Yellow leaflets after recrystallization from alcohol, m.p. 155°.

The methyl ester of the acid was prepared from its silver salt and methyl iodide. The silver salt was obtained by treatment of an aqueous solution of the acid with an equivalent amount of silver oxide and evaporation of the solution obtained. 2.8 g of finely powdered dry silver salt was heated at 100° in a sealed tube for 10 hours

with an excess of methyl iodide. The methyl iodide was distilled off and the residue treated with 10 ml boiling toluene. The boiling toluene solution was filtered and the methyl ester precipitated on cooling. A second crystallization from toluene yielded 1.5 g (73%); colorless prisms with m.p. 86-87°. An attempt to prepare the same ester by the action of a solution of sodium in methyl alcohol on a solution of the sulfonyl chloride in absolute ether at −5° was unsuccessful. A small amount of methyl 2-hydroxy-5-nitrobenzenesulfonate with m.p. 95-97° was isolated from the mixture of products after several crystallizations from ether.

Found %: N 5.98, 5.97. $C_7H_7O_6NS$. Calculated %: N 6.01.

2,3-Dinitrobenzenesulfonic acid was prepared from 2,3-dinitroaniline by a similar method to that by which 2,5-dinitrobenzenesulfonic acid was prepared. Yield 44%. The acid is soluble in water, alcohol, acetone, insoluble in ether and benzene. The potassium salt was prepared by the action of potassium carbonate on the acid in aqueous solution – light yellow needles (from water).

The methyl ester was prepared from the silver salt, 6 g of which yielded 3.3 g (75%) of the ester, m.p. 153°, after crystallization from a mixture of benzene and ether.

3,4-Dinitrobenzenesulfonic acid was prepared in the same way as the previous dinitrobenzenesulfonic acids. Since it is not precipitated from nitric acid solution, the mixture after oxidation was diluted with 300 ml water, the solution filtered and evaporated on the water bath to remove the nitric acid. When the dilution and evaporation had been carried out three times a solid yellow product was obtained. The sulfonic acid is soluble in water and alcohol, sparingly soluble in ether and insoluble in benzene. It was converted into its potassium salt by the action of potassium carbonate. 19 g (59%) of the potassium salt was obtained from 20.59 g of 3,4-dinitroaniline after recrystallization from water.

The chloride was prepared from 4.9 g of the potassium salt dried at 140° and 10 g phosphorus pentachloride. The mixture was heated at 145-150° for 1 hour and then poured on to ice. (When the chloride did not solidify by this treatment, it had to be extracted with ether, the ether solution washed with water, dried with calcium chloride and the ether distilled off). When recrystallized from a small quantity of ether 3.5 g (77%) of the sulfonyl chloride with m.p. 59° was obtained.

The amide was obtained by the action of ammonia on an ethereal solution of the sulfonyl chloride. Unlike 2,5-dinitrobenzenesulfonamide, it is insoluble in aqueous ammonia. Yellow leaflets with m. p. 165-166° after crystallization from 50% alcohol.

The methyl ester was prepared from the sulfonyl chloride and sodium methoxide. A solution of 0.39 g sodium in 7 ml anhydrous methyl alcohol was added with stirring at −5° to a solution of 4.5 g sulfonyl chloride in 50 ml absolute ether. The residue after evaporation of the ether at room temperature was treated with ice water, the product dried and recrystallized from toluene. Yield 1.8 g (41%); colorless leaflets with m.p. 91-92°

2-Nitro-4-trifluoromethylbenzenesulfonic acid. 10 g of 4,4'-bis-trifluoromethyl-2,2'-dinitrodiphenyl disulfide [9] was added in small portions to 30 ml nitric acid (d 1.5). Vigorous evolution of oxides of nitrogen was observed and the disulfide passed into solution. The mixture was then heated for 2 hours on the water bath, the solution diluted with 5 times its volume of water, filtered, diluted with water and evaporated on the water bath several times to remove the nitric acid and finally evaporated to dryness. 12.8 g of the sulfonic acid was obtained.

The methyl ester of the acid was prepared in the same way as methyl 2,5-dinitrobenzenesulfonate. Yield from 3 g of the silver salt 1.75 g (72%), m.p. 86-87°.

The esters of 2,4-dinitrobenzenesulfonic acid. 2,4-Dinitrobenzenesulfonyl chloride was prepared by heating 2,4-dinitrobenzenesulfonic acid, dried at 120°, with an equal weight of phosphorus pentachloride for 1.5 hours on a water bath. M.p. 102° (according to [10] 102°). A solution of 0.46 g sodium in 10 ml methyl alcohol was added with stirring to a solution of 5.32 g 2,4-dinitrobenzenesulfonyl chloride in 30 ml toluene cooled to −5°. The solution was then raised gradually with stirring to room temperature and filtered. Benzene was added to the filtrate until a suspension appeared. The solution was left for several hours at 0°. The product which precipitated was purified by crystallization from toluene. Yield of methyl ester 2.6 g (50%), m.p. 86.5°. The ethyl ester was prepared in the same way, yield 42%; needles, m.p. 97°. The phenyl ester was prepared in the same way from 4 g of the sulfonyl chloride and 1.74 g of anhydrous sodium phenoxide in toluene. The ester was precipitated with benzene and crystallized from methyl alcohol. Yield 3 g (62%), m.p. 115-116°. The o-nitrophenyl ester was synthesized similarly, yield 63%, m.p. 139°.

The esters of 3, 5-dinitrobenzenesulfonic acid. 3, 5-Dinitrobenzenesulfonyl chloride was prepared from the barium salt of the sulfonic acid [11] and phosphorus pentachloride at 150° in 63% yield, m.p. 102° (according to the literature data 98-99° [12]). A solution of 1.15 g sodium in 10 ml methyl alcohol was added with stirring at -10° to a solution of 13.3 g of the sulfonyl chloride in 90 ml toluene. The mixture was stirred at the same temperature for a further hour. The product was separated by filtration, washed with ice water and crystallized from toluene. Yield of methyl ester 8.8 g (67%), needles, m.p. 162°. The cyclohexyl ester was prepared similarly. It was separated by diluting the mixture with benzene. Yield 36%, m.p. 81-83° (with decomp.). The ester may be crystallized from toluene, but in this case the temperature must not be raised above 60°, otherwise decomposition takes place to cyclohexene and the sulfonic acid.

The esters of 2-nitro 4-chlorobenzenesulfonic acid. Chlorine was passed for 2 hours with stirring through a mixture of 6.21 g 2, 2'-dinitro-4, 4'-dichlorodiphenyl disulfide [2], 25 ml hydrochloric acid and 5 ml nitric acid (d 1.42) heated to 70-75°. The liquid was then decanted and the product remaining treated twice with water heated to 75 80°. The sulfonyl chloride was separated by filtration, dissolved in 50 ml glacial acetic acid, the solution filtered and the sulfonyl chloride precipitated by the addition of water. Yield of 2-nitro-4-chlorobenzenesulfonyl chloride 7.1 g (84%), m.p. 74-75° (75° according to [13]). The esters of 2-nitro-4-chlorobenzenesulfonic acid were prepared from the sulfonyl chloride described and the appropriate alkoxide in ether at 0°. Methyl ester—yield 62%, needles (from a mixture of benzene and benzole), m.p. 101-102°. Ethyl ester—needles (from benzene and benzole), m.p. 97.5°. n-Propyl ester—needles (from benzene), m.p. 63°. Isopropyl ester—needles (from benzene), m.p. 59-60°.

The esters of p-nitrobenzenesulfonic acid. 140 ml nitric acid (d 1.5) was added dropwise with mechanical stirring to 50 g p-nitrothiophenol [14]. The reaction mixture was then heated for 15 minutes on the gauze, diluted with 0.5 liters of water, the solution filtered and the filtrate evaporated. The sulfonic acid obtained after a second dilution and evaporation was converted, by the action of potassium carbonate on its aqueous solution, into the potassium salt, 48.2 g (62%) of which was obtained after drying at 120°. This was converted into the sulfonyl chloride [15]. The esters of p-nitrobenzenesulfonic acid were prepared in the same way as the esters of 2 nitro-4-chlorobenzenesulfonic acid, but at room temperature. N-Octyl ester—leaflets (from benzene), yield 50%, m.p. 73°. Cyclohexyl ester—needles (from benzene), yield 54%, m.p. 78° (with decomp.).

Trimethyleneglycol di-o-nitrobenzenesulfonate was prepared by stirring a solution of o-nitrobenzenesulfonyl chloride with monosodium trimethyleneglycol for 12 hours at room temperature. Yield 6%, needles (from toluene), m.p. 110°.

SUMMARY

A description is given of the synthesis of 2, 3-, 2, 5- and 3, 4-dinitro-, 2-nitro-4-trifluoromethylbenzenesulfonic acids and a number of their derivatives. Esters of these acids have been prepared, together with several esters of 2, 4- and 2, 5-dinitro-, 2-nitro-4-chlorobenzenesulfonic acids and of o- and p-nitrobenzenesulfonic acids.

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THE PREPARATION OF LINEAR POLYETHYLSILOXANES

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Methylsiloxane polymers have been described repeatedly in the literature. Patnode and Wilcock [1] isolated polymethylsiloxanes of general formula $[(CH_3)_2SiO]_n$, with from 3 to 8 silicon atoms in the molecule, from the product of the hydrolysis of dimethyldichlorosilane. They also prepared a number of linear polymers of formula $(CH_3)_3Si[OSi(CH_3)_2]_mSi(CH_3)_3$, where m = 1-3, by treating a mixture of octamethylcyclotetrasiloxane and hexamethyldisiloxane with concentrated sulfuric acid. Hunter [2] prepared linear polymethylsiloxanes, containing from 2 to 7 silicon atoms in the molecule, by the simultaneous hydrolysis of dimethyldiethoxysilane and trimethylethoxysilane in the presence of alkali and subsequent rearrangement with 20% hydrochloric acid. Lewis [3] isolated trimethyltriphenylcyclotrisiloxane from the product of the hydrolysis of methylphenyldichlorosilane, and also prepared tetramethyl-1, 3-diphenyldisiloxane, pentamethyl-1, 3, 5-triphenyltrisiloxane and heptamethyl-3-phenyltrisiloxane. Joung [4] prepared hexaethylcyclotrisiloxane and octaethylcyclotetrasiloxane by the hydrolysis of an ethereal solution of diethyldichlorosilane and subsequent treatment of the hydrolysis product with 5% caustic soda solution. Hard and Osthoff [5] have prepared and isolated decaethylcyclopentasiloxane.

Ethylsiloxane polymers of linear structure have not as yet been described in the literature. In the present work a method is given for the synthesis and isolation of ethylsiloxane polymers of linear structure with from 3 to 5 silicon atoms in the molecule.

EXPERIMENTAL

To prepare linear ethylpolysiloxanes, the method used was catalytic rearrangement in the presence of aluminosilicate [6]. The starting materials used were hexaethylcyclotrisiloxane, octaethylcyclotetrasiloxane and hexaethyldisiloxane.

The synthesis of the starting materials. The starting material for the preparation of hexaethylcyclotrisiloxane and octaethylcyclotetrasiloxane was pure diethyldichlorosilane, which was hydrolyzed by water according to the scheme:

$$n(C_2H_5)_2SiCl_2 + nH_2O \longrightarrow [(C_2H_5)_2SiO]_n + 2nHCl.$$

480 g of ice was added in small portions to a mixture of 240 g diethyldichlorosilane and 350 ml diethyl ether. When all the ice had melted, the mixture was heated to boiling point and kept at that temperature under reflux for 1 hour. The aqueous layer was then separated, the ether layer washed with an equal volume of water and heated for 1 hour at the boiling point with 50 ml 5% caustic soda solution. The alkaline layer was removed, the ethereal solution of the mixture of polyethylsiloxanes washed with water until neutral to phenolphthalein and the ether distilled off. The yield of hydrolysis product amounted to 148 g (95%). The individual compounds were isolated from the hydrolysis product by fractional distillation. Hexaethyldisiloxane was prepared from triethylchlorosilane by hydrolysis with an equal volume of water according to the scheme:

$$2(C_2H_5)_3SiCl + H_2O \longrightarrow (C_2H_5)_3SiOSi(C_2H_5)_3 + 2HCl.$$

The hydrolysis product was washed with water, treated with 4% by volume of concentrated sulfuric acid with stirring for 6 hours, washed again with water, dried with calcium chloride and fractionally distilled.

The separation of the individual polymers from the hydrolysis products was carried out by fractional distillation on a film column with an efficiency of 20 theoretical plates. The rectifying part of the column consisted of two concentric tubes with diameters 12 and 14 mm and length 600 mm. The circular opening between the tubes was 1 mm wide. To achieve adiabatic conditions for the separation process the column was placed in a metal jacket filled with insulating material and fitted with a two-section electric heater. Temperature control according to the height of the column was achieved using a chromel-alumel thermocouple and potentiometer. The temperature of the still and the distillate were measured using thermometers with an accuracy of 0.2°. In the rectification of hexaethyldisiloxane the rate of flow of liquid in the circular opening was kept within the limits 200-250 ml/hour and the reflux number was 10-15. The yield of hexaethyldisiloxane was 85% of the mixture taken for rectification. The product had b.p. 72-73° (1 mm), n_D^{20} 1.4340, M 240.

Found %: C 58.49; H 12.50; Si 22.80. $C_{12}H_{30}OSi_2$. Calculated %: C 58.66; H 12.20; Si 22.76.

The rectification of the cyclic polymers was carried out at the same rate of liquid flow, but the reflux number in the distillation process was 25-30. 41% of a fraction boiling at 91° (hexaethylcyclotrisiloxane) and 31% of a fraction boiling at 127° (octaethylcyclotetrasiloxane) were isolated. The properties of the compounds obtained are given in Table 1.

TABLE 1

Composition (%) and properties of the products	Hexaethylcyclotrisiloxane			Octaethylcyclotetrasiloxane		
	found	calc.	literature data [4]	found	calc.	literature data [4]
Carbon	47.0	47.0	—	47.1	47.0	—
Hydrogen	10.27	9.88	—	10.27	9.88	—
Silicon	27.65	27.45	—	27.54	27.45	—
Molecular wt.	296	306	—	404	408	—
Refractive index (n_D^{20})	1.4308	—	1.4308	1.4338	—	1.4338
Specific gravity (d_4^{20})	0.9550	—	0.9549	0.9630	—	0.9640
Molecular refraction (MR_D)	82.9	83.7	—	110.3	111.1	—
Viscosity at 20° (in centistokes)	3.6	—	3.6	11.1		11.2

The synthesis of linear ethylsiloxane polymers. For the preparation of linear ethylsiloxane polymers by catalytic rearrangement, the components required were calculated according to the equation:

$$(C_2H_5)_3SiOSi(C_2H_5)_3 + \frac{1}{n}[(C_2H_5)_2SiO]_n \longrightarrow (C_2H_5)_3SiOSi(C_2H_5)_2OSi(C_2H_5)_3 .$$

20.4 g octaethylcyclotetrasiloxane (or hexaethylcyclotrisiloxane) and 49.2 g hexaethyldisiloxane were placed in a reaction flask fitted with stirrer, thermometer and reflux condenser. The liquid was heated to 120° on an oil bath and 5.6 g aluminosilicate added with stirring. The mixture was stirred at 120° for 5 hours (until the liquid phase had a constant viscosity) and filtered while still hot through a paper filter on a Buchner funnel to remove the aluminosilicate.

The product of the rearrangement had the following characteristics:

Found %: C 55.67; H 11.76; Si 24.40. M351. $C_{16}H_{40}O_2Si_3$. Calculated %: C 55.20; H 11.50; Si 24.30. M348.

The mixture of linear polymers obtained was distilled on a column at a residual pressure of 1 mm. The yields and characteristics of the polymers obtained are given in Table 2.

TABLE 2

Composition (%) and Properties of the Products	Octaethyltrisiloxane		Decaethyltetrasiloxane		Dodecaethylpentasiloxane	
	found	calculated	found	calculated	found	calculated
Boiling point (1 mm)	113–114°	—	151°	—	188–189°	—
Yield (%)	23.5	—	15.5	—	2.7	—
Refractive index (n_D^{20})	1.4389	—	1.4415	—	1.4445	—
Specific gravity (n_D^{20})	0.8940	—	0.9121	—	0.9252	—
Molecular refraction (MR_D)	102.8	104.1	130.4	131.9	158.6	159.7
Molecular weight	338	348	451	450	555	552
Carbon	55.3	55.2	53.3	53.4	52.1	52.2
Hydrogen	11.6	11.5	11.5	11.2	11.0	11.0
Silicon	24.4	24.3	24.8	24.9	25.2	25.4

SUMMARY

New ethylsiloxane linear polymers with the general formula $(C_2H_5)_3SiO[Si(C_2H_5)_2O]_nSi(C_2H_5)_3$, where n = 1, 2 and 3, have been prepared.

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THE REACTION OF CHLOROFORM, BROMOFORM AND SILICOCHLOROFORM WITH SODIUM TRIPHENYLSILANOLATE

V. S. Chugunov

It has been shown by us earlier [1] that, depending on the conditions, the reaction of silicon tetrachloride with sodium triphenylsilanolate may take place either stepwise with the formation of triphenyltrichlorodisiloxane, bis-(triphenylsiloxy)dichlorosilane or tris-(triphenylsiloxy)chlorosilane, or, when excess sodium triphenylsilanolate is used, with the formation of tris-(triphenylsiloxy)chlorosilane according to the equation:

$$3(C_6H_5)_3SiONa + SiCl_4 = [(C_6H_5)_3SiO]_3SiCl + 3NaCl.$$

Attempts to prepare tetrakis-(triphenylsiloxy)silane in the same way as tetrakis-(trialkylsiloxy)silanes [2-4] gave no positive result even when the more reactive tris-(triphenylsiloxy)fluorosilane was boiled with excess sodium triphenylsilanolate.

The primary aim of the present work was the study of the reaction of sodium triphenylsilanolate with carbon tetrachloride. When the latter was boiled for 16 hours with sodium triphenylsilanolate (in the molar ratio 1:4), however, the expected result was not obtained. When the carbon tetrachloride was replaced by chloroform or bromoform, the formation of tris-(triphenylsiloxy)methane took place. Their analog–silicochloroform–reacted smoothly with sodium triphenylsilanolate with the formation of triphenyldichlorodisilanoxane, bis-(triphenylsiloxy)chlorosilane and tris-(triphenylsiloxy)silane. When tris-(triphenylsiloxy)silane was treated with a solution of alkali, the hydrogen situated on the silicon atom, as in the case of the trialkyl- or arylsilanes, was quantitatively replaced by the hydroxyl group with the formation of tris-(triphenylsiloxy)silanol according to the scheme:

$$[(C_6H_5)_3SiO]_3SiH \xrightarrow[(HOH)]{NaOH} [(C_6H_5)_3SiO]_3SiOH + H_2.$$

EXPERIMENTAL

Tris-(triphenylsiloxy)methane. 3.5 g chloroform was added with cooling by ice water to a solution of sodium triphenylsilanolate prepared from 26.7 g triphenylsilanol in 150 ml benzene and 2.5 g sodium, and the mixture boiled for 8 hours. After removal of sodium chloride the crystals obtained were recrystallized twice from benzene.

16.5 g (60% yield) was obtained (m.p. 222-223°).

Found %: C 78.40, 78.64; H 5.62, 5.57; Si 10.11, 10.23. $C_{55}H_{46}O_3Si_3$. Calculated %: C 78.81; H 5.52; Si 10.04.

Tris-(triphenylsiloxy)methane, identified by its melting point, was obtained (in 71% yield) under similar conditions from 4.2 g bromoform, 14 g triphenylsilanol and 1.3 g sodium.

Triphenyldichlorodisiloxane. Sodium triphenylsilanolate was prepared from 41.5 g triphenylsilanol in 400 ml benzene and 4 g sodium. The solution was cooled, 23.5 g silicochloroform added and the mixture boiled for 4 hours. The sodium chloride was removed and the filtrate fractionated. 29.4 g triphenyldichlorodisiloxane (87.5% yield, calculated on the triphenylsilanol) was collected in the form of a transparent oily liquid with b.p. 345-350°, d_4^{20} 1.1908, n_D^{20} 1.576.

Found %: C 57.77, 57.41; H 4.62, 4.61; Cl 19.1, 19.0; Si 14.6, 14.71. $C_{18}H_{16}OCl_2Si$. Calculated %: C 57.59; H 4.29; Cl 18.9; Si 14.95.

Bis-(triphenylsiloxy)chlorosilane. Sodium triphenylsilanolate was prepared from 9 g triphenylsilanol in 200 ml benzene and 0.8 g sodium. 11.3 g triphenyldichlorodisiloxane was added and the mixture boiled for 4 hours. The sodium chloride was removed and the solution evaporated to half its original volume to yield 12.2 g (66%) bis-(triphenylsiloxy)chlorosilane with m.p. 145-146° (from benzene).

Found %: Si 13.3, 13.5; Cl 5.2, 5.3. M 620, 614, $C_{36}H_{31}O_2ClSi_3$. Calculated %: Si 13.7; Cl 5.7. M 615.

Tris-(triphenylsiloxy)silane was synthesized by two methods:

a) 6.1 g bis-(triphenylsiloxy)chlorosilane was added to sodium triphenylsilanolate prepared from 7.5 g triphenylsilanol in 100 ml benzene and sodium. The solution was boiled for 3 hours and the sodium chloride removed to yield 8.4 g tris-(triphenylsiloxy)silane with m.p. 211-212° (from benzene).

Found %: C 78.86, 78.59; H 5.60, 5.73; Si 10.26, 9.94. $C_{54}H_{46}O_3Si_4$. Calculated %: C 78.4; H 5.6; Si 10.2

b) Sodium triphenylsilanolate was prepared from 13.8 g triphenylsilanol and 1.5 g sodium. The solution was cooled to 0° and 2.3 g silicochloroform added; the mixture was boiled for 4 hours. 7.8 g (54%, calculated on the silicochloroform) of tris-(triphenylsiloxy)silane, identified by its melting point, was obtained.

Determination of hydrogen. The presence of hydrogen bound directly to the silicon atom in tris-(triphenylsiloxy)silane was established by the method of Price [5], based on the replacement of the hydrogen in R_3SiH by a hydroxyl group in alkaline medium. 0.6428 g tris-(triphenylsiloxy)silane was dissolved in 30 ml dry acetone in a Tserevitinov apparatus and 30 ml 20% caustic soda solution added. 8.1 ml of H_2 was collected; calculated value 8.4 ml H_2. When 0.9642 g of substance was treated with alkali, 12.2 ml H_2 was collected; calculated value 12.6 ml H_2. The tris-(triphenylsiloxy)silanol (m.p. 242-243°), recrystallized from benzene, was identified by taking a mixed melting point with a sample of the product prepared by us earlier [1].

SUMMARY

1. Tris-(triphenylsiloxy)methane has been prepared for the first time in good yield (60-70%) from chloroform or bromoform and sodium triphenylsilanolate.

2. It has been shown that silicochloroform, like silicon tetrachloride, reacts smoothly with sodium triphenylsilanolate with the formation of triphenyldichlorodisiloxane, bis-(triphenylsiloxy)chlorosilane and tris-(triphenylsiloxy)silane.

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THE REDUCTION OF MERCURATED AMIDES OF CARBOXYLIC ACIDS WITH ESTERS OF PHOSPHOROUS ACID

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The reduction of mercury salts of carboxylic acids with esters of phosphorous acid [1] leads to the formation of esters according to the following scheme:

$$(CH_3COO)_2Hg + P(OR)_3 \longrightarrow Hg + [(CH_3COO)_2P(OR)_3]$$
$$\downarrow$$
$$2CH_3COOR + (ROPO_2)_X.$$

The trialkyl phosphite thus behaves in this reaction as an alkylating agent.

In the present article the results are given of a study of the reaction of trialkyl phosphites with mercurated amides of carboxylic acids. In this reaction, too, metallic mercury is liberated quantitatively; the amide residue, however, is not alkylated in the process. Instead of the alkylated amide, the products obtained in good yield are the trialkyl phosphate and the amide and nitrile of the carboxylic acid. The reaction was studied with the mercurated amides of acetic, propionic, isobutyric and benzoic acids and may be represented by the following scheme:

$$(RCONH)_2Hg + P(OR')_3 \rightarrow Hg + \left[\begin{array}{c} RCONH \\ RCONH \end{array}\!\!>\!P\!\begin{array}{l} \diagup OR' \\ -OR' \\ \diagdown OR' \end{array}\right].$$

Under the conditions of the reaction, the amide of the acid is split off from the compound formed:

$$\left[\begin{array}{c} RCONH \\ RCONH \end{array}\!\!>\!P\!\begin{array}{l} \diagup OR' \\ -OR' \\ \diagdown OR' \end{array}\right] \rightarrow RCONH_2 + RCON = P(OR')_3.$$

The reaction between the mercurated amide of the carboxylic acid and the trialkyl phosphite takes place with considerable evolution of heat. To separate the metallic mercury completely the reaction mixture was boiled for five minutes. Under these conditions the trialkoxyphosphazoacyls, formed after the removal of the molecule of the amide of the carboxylic acid, undergo further decomposition to the trialky phosphate and the nitrile of the carboxylic acid:

$$RCON = P(OR')_3 \longrightarrow RCN + OP(OR')_3.$$

An analogous phosphazo compound decomposition was first described by Staudinger [2]; thus, by heating triethylphosphinebenzoylimine to 120°, he obtained triethylphosphine oxide and benzonitrile:

$$C_6H_5CON = P(C_2H_5)_3 \longrightarrow C_6H_5CN + OP(C_2H_5)_3.$$

The same type of phosphazo compound decomposition was recently described with trichlorophosphazoacyls as examples [3]:

$$C_6H_5CON = PCl_3 \longrightarrow C_6H_5CN + OPCl_3.$$

A. V. Kirsanov replaced the chlorine atoms in $C_6H_5CON = PCl_3$ by phenoxy groups by treating the compound in benzene solution with sodium phenoxide. The triphenyl ester of benzoylimidophosphoric acid obtained proved to be unstable and on distillation or on storing for a week at room temperature in the presence of traces of hydrogen chloride decomposed quantitatively to benzonitrile and triphenyl phosphate.

A similar thermal instability is evidently shown by the esters of acylimidophosphoric acid whose intermediate formation has been postulated by us.

EXPERIMENTAL

The mercurated amides of the carboxylic acids were prepared by fusing mercuric oxide with the carboxylic acid amide [4].

In preparation of mercurated isobutyramide. 17.4 g isobutyramide and 21.6 g mercuric oxide were mixed. The mercuric oxide dissolved on gradual heating. The mercurated isobutyramide obtained was crystallized from water. Yield 35 g (95%); m.p. 152-153°.

Found %: Hg 51.67, 51.78. $C_8H_{16}O_2N_2Hg$. Calculated %: Hg 51.33.

The reaction of mercuracetamide with tributyl phosphite. 25 g tributyl phosphite was added to 31.6 g mercuracetamide. The reaction began immediately and proceeded with the evolution of heat. The mixture was boiled for five minutes and the fraction with b.p. 74-85° distilled off. A second distillation of this fraction yielded acetonitrile with the following constants: b.p. 79-81°, n_D^{20} 1.3455. Yield 3.25 g (80%). According to [5], b.p. 81°, n_D^{20} 1.3460. Metallic mercury was isolated from the residue in the Wurtz flask; yield 20 g (100%).

When the residue was vacuum distilled the following fractions were obtained: 1st 93-96° (6 mm), 5.4 g; 2nd 137-139° (6 mm), 13 g. The 1st fraction proved to be acetamide, b.p. 81°; yield 91%. The 2nd fraction was tributyl phosphate; yield 48% n_D^{20} 1.4248. According to [6], b.p. 138° (6 mm), n_D^{20} 1.4249.

Found %: C 53.80, 54.15; H 9.92, 10.42; P 11.58, 11.39. $(C_4H_9O)_3PO$. Calculated %: C 54.12; H 10.22; P 11.62.

The reaction of mercurated propionamide with tributyl phosphite. 14.4 g tributyl phosphite was added to 20 g mercurated propionamide. The mixture was boiled for five minutes and a fraction with b.p. 80-110° distilled off. A second distillation yielded propionitrile with b.p. 97-98°, n_D^{20} 1.3710; yield 3.2 g (77%). According to [5], b.p. 98°, n_D^{20} 1.3681. Metallic mercury (11 g, 95%) was isolated from the residue which was then distilled. The following fractions were collected: 1st 92-93° (3 mm), 2.6 g; 2nd 130-131° (3 mm), 6.5 g. 1st fraction—propionamide; yield 62%; m.p. 78°. 2nd fraction—tributyl phosphate; yield 43%; n_D^{20} 1.4249.

The reaction of mercurated isobutyramide with tributyl phosphite. 12.5 g tributyl phosphite was added to 18.6 g mercurated isobutyramide. The mixture was boiled for five minutes and a fraction with b.p. 95-110° was distilled from the Wurtz flask. A second distillation yielded isobutyronitrile with b.p. 106-108°; n_D^{20} 1.3700; yield 5.4 g (77%). According to [5], b.p. 106-108°, n_D^{20} 1.3713. The metallic mercury (10 g, 100%) was removed from the residue which was then distilled. The following fractions were collected: 1st 74-76° (5 mm), 1 g; 2nd 136-138° (5 mm), 4.1 g. 1st fraction—isobutyramide; yield 13%; m.p. 128°. The low yield of isobutyramide is explained by the considerable decomposition which takes place when this compound is heated or distilled. 2nd fraction—tributyl phosphate; yield 30%; n_D^{20} 1.4247.

The reaction of mercurated benzamide with tributyl phosphite. 5 g tributyl phosphite was added to 8 g mercurated benzamide. The mixture was heated for five minutes and a fraction with b.p. 180-200° distilled from the Wurtz flask. A second distillation yielded benzonitrile with b.p. 190-191°; yield 1 g (54%). Metallic mercury (3.6 g, 100%) was removed from the residue in the Wurtz flask and the benzamide filtered off (0.9 g, 41%), m.p. 127° (from water). Vacuum distillation yielded 3.4 g tributyl phosphate with b.p. 140-142° (8 mm) slightly contaminated with benzamide.

SUMMARY

It has been found that the reaction of mercurated amides of carboxylic acids with esters of phosphorous acid leads to the liberation of metallic mercury and the formation of the amide and nitrile of the carboxylic acid together with the phosphoric acid ester. It is suggested that the reaction takes place via an intermediate stage involving the formation of the ester of the acylimidophosphoric acid.

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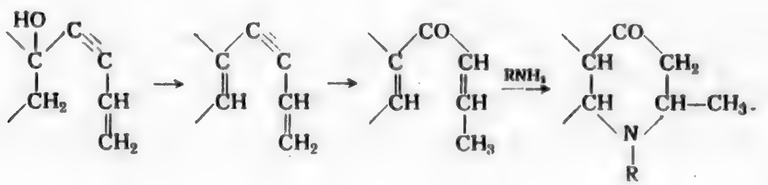
HETEROCYCLIC COMPOUNDS

52. THE SYNTHESIS OF 1-γ-ALKOXYPROPYL-4-PIPERIDONES AND 1-γ-DIALKYLAMINOPROPYL-4-PIPERIDONES

I. N. Nazarov and S. M. Makin

A simple method has recently been worked out in our laboratory for the synthesis of various γ-piperidones by the reaction of ammonia or primary amines with vinyl propenyl ketones obtained by the hydration of divinylacetylenic hydrocarbons in aqueous methanol solutions [1-3]:



In this way a wide variety of γ-piperidones may be prepared with mono-, di- and polycyclic structures, containing different aliphatic, alicyclic and aromatic radicals in the piperidine ring [4-6].

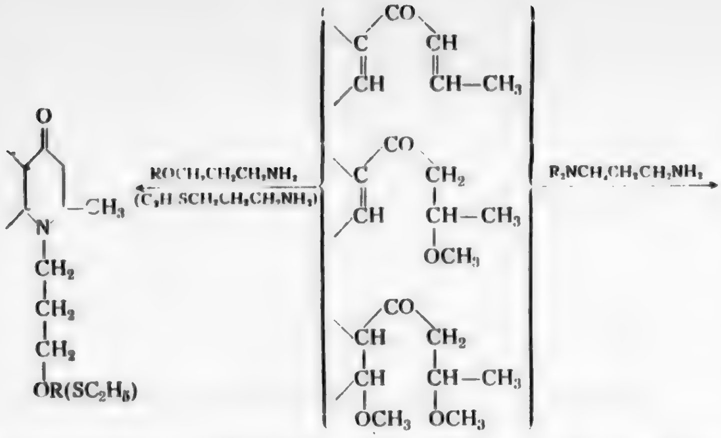
Taking into consideration the great importance of γ-piperidones for the synthesis of new physiologically active compounds, showing, in particular, a powerful pain-relieving, anesthetic and antispasmodic action, we have now studied the reaction of vinyl propenyl ketones with γ-dialkylaminopropylamines, γ-alkoxypropylamines and γ-ethylmercaptopropylamine, which are readily obtained from acrylonitrile according to the following scheme:

$$CH_2{=}CH{-}CN \xrightarrow{R_2NH} R_2NCH_2CH_2CN \xrightarrow{H_2;\,Ni} R_2NCH_2CH_2CH_2NH_2\ [7]$$

$$CH_2{=}CH{-}CN \xrightarrow{ROH} ROCH_2CH_2CN \xrightarrow{H_2;\,Ni} ROCH_2CH_2CH_2NH_2\ [8]$$

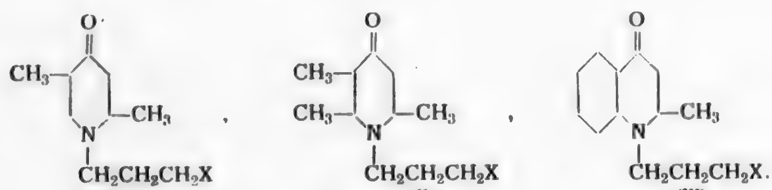
$$CH_2{=}CH{-}CN \xrightarrow{C_2H_5SH} C_2H_5SCH_2CH_2CN\ [9] \xrightarrow[(C_2H_5OH+Na)]{H} C_2H_5SCH_2CH_2CH_2NH_2.$$

It turned out that the various vinyl propenyl ketones react with the above amines even more readily than with ordinary alkylamines, giving the corresponding γ-piperidones in yields of up to 90%:



Instead of vinyl propenyl ketones, the corresponding β-methoxyketones, formed as a result of the addition of methanol to the vinyl propenyl ketones (in the process of hydration of the diene-ines in aqueous methanol solutions) may be used in this reaction with equal success.

In this way we have prepared more than twenty new γ-piperidones and 2-methyl-4-ketodecahydroquinolines of the following three types:



(I) (II) (III)

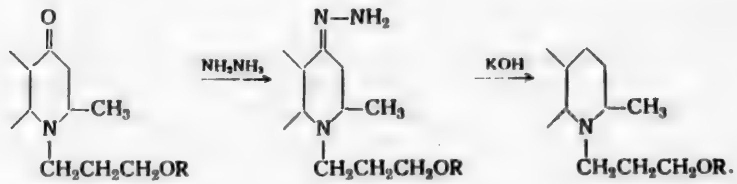
$X = CH_3O,\ C_2H_5O,\ n\text{-}C_3H_7O,\ n\text{-}C_4H_9O,\ C_2H_5S,\ (CH_3)_2N,\ (C_2H_5)_2N,\ (CH_2)_5N.$

The γ-piperidones obtained will later be used for the synthesis of various piperidine derivatives with the aim of finding new physiologically active compounds and medicinal products.

It is interesting to note that the reactions of the β-methoxyketones with the above amines takes place readily even at room temperature, but only in the presence of water (yield of γ-piperidones 70-90%), whereas in anhydrous conditions the reaction takes place with great difficulty and is not complete even after prolonged heating (yield of γ-piperidones 20-30%). The same powerful accelerating influence of water on similar reactions has been observed earlier in a number of different examples [6].

Unlike the β-methoxyketones, but in the same way as the α, β-unsaturated ketones, the vinyl propenyl ketones themselves react readily with amines in anhydrous conditions also. Consequently, the role of water in these reactions is explained by the fact that it facilitates the removal of the alcohols from the β-alkoxyketones with the formation of the α, β-unsaturated ketones, which then react with the amines. The fact that the alcohols are removed from the β-alkoxyketones under the influence of aqueous solutions of amines at room temperature has been established in our laboratory for a number of examples [6]. The cyclization of vinyl propenyl ketones, and also of the β-alkoxyketones corresponding to them, takes place more readily, the greater the basic strength of the primary amine taken for the reaction with these ketones. The reaction takes place most readily with γ-dialkylaminopropylamines (at room temperature, yield up to 90%) and with greatest difficulty with aniline and other primary aromatic amines [6]. In the latter case the reaction may stop at the stage of the addition of the amine to the double bond with the formation of the corresponding open-chain aminoketone.

Several of the γ-piperidones prepared by us were reduced to the corresponding piperidine bases using hydrazine hydrate (according to Kizhner [10]):



EXPERIMENTAL

Propenyl isopropenyl ketone and the corresponding methoxyketones (b.p. 57-63° at 10 mm, n_D^{20} 1.4520) were obtained by the hydration of vinylisopropenylacetylene in aqueous methanol solutions in the presence of mercuric sulfate, as described earlier [1].

5-Methyl-2, 5-heptadiene-4-one (b.p. 72-75° at 7 mm, n_D^{20} 1.4825) [2] was prepared similarly be dehydration of 5-methyl-1, 5-heptadiene-3-ine.

Propenyl Δ'-cyclohexenyl ketone (b.p. 105-107° at 7 mm, n_D^{20} 1.5160) was prepared by hydration of vinyl-Δ'-cyclohexenylacetylene [3].

β-Dialkylaminopropionitriles

320 g of freshly distilled acrylonitrile was added in small portions with uninterrupted stirring to 1 kg of 35% aqueous methylamine solution at such a rate that the reaction temperature remained steady at 40-45°. When all the acrylonitrile had been added, the reaction mixture was left at room temperature for 40 minutes and then saturated with alkali. The oil which rose to the surface was removed, the aqueous layer extracted with ether and the product dried with ignited sodium sulfate. 492 g (82%) of β-dimethylaminopropionitrile with b.p. 169-172° was obtained after distillation.

In the same way good yields were obtained of β-diethylaminopropionitrile with b.p. 86-88° (20 mm) [5] and β-(N-piperidyl)-propionitrile with b.p. 114-115° (18 mm) [11].

β-Alkoxypropionitriles

180 g methyl alcohol was added in small portions with uninterrupted stirring to a mixture of 225 g acrylonitrile and several drops of concentrated sodium methoxide prepared by dissolving 1.5 g metallic sodium in 20 ml methyl alcohol and then evaporating in vacuo to ⅓ of the initial volume, the addition of the methyl alcohol taking place at such a rate that the reaction temperature did not exceed 40-45°. The mixture was left overnight at room temperature and next day it was acidified with acetic acid and distilled. 288 g (80.5%) β-methoxypropionitrile with b.p. 162-164° was obtained [8].

The following nitriles were obtained in the same way [8]: β-ethoxypropionitrile with b.p. 169-172° (yield 78%), β-n-propoxypropionitrile with b.p. 85-89° at 24 mm (yield 95%), β-n-butoxypropionitrile with b.p. 74-75° at 10 mm (yield 85.5%), β-ethylmercaptopropionitrile with b.p. 100° at 13 mm (yield 95%).

γ-Alkoxypropylamines

425 g β-methoxypropionitrile (b.p. 163-164°) was dissolved in 500 ml methyl alcohol, saturated with ammonia with cooling by a mixture of snow and salt and then hydrogenated in an autoclave over Raney nickel catalyst (25 g) at a temperature of 95-100° and a hydrogen pressure of 90-120 atm. The theoretical quantity of hydrogen was absorbed in 2 hours. Repeated distillation of the product in a Favorsky flask with fractionating column of height 30 cm yielded 270 g (63.5%) γ-methoxypropylamine with b.p. 117-119° (734 mm).

The following amines were obtained in the same way [8]: γ-ethoxypropylamine with b.p. 133-136° (yield 50%), γ-n-propoxypropylamine with b.p. 153-156° (yield 50%), γ-n-butoxypropylamine with b.p. 74-76° at 21 mm (yield 71%).

γ-(Ethylmercapto)-propylamine

40 g metallic sodium was dispersed using a mechanical stirrer in 150 ml anhydrous toluene at 105° in a three-necked flask fitted with reflux condenser and dropping-funnel. 36 g of β-ethylmercaptopropionitrile in 200 ml anhydrous ethyl alcohol was then added with vigorous stirring over a period of 45 minutes. To dissolve the unreacted metallic sodium, a further 50 ml ethyl alcohol was added and 150 ml water added to the mixture. The reaction mass was acidified to congo red with hydrochloric acid and the alcohol and the greater part of the water distilled off in vacuo. The residue was washed with ether and treated with solid alkali. The reaction product was carefully extracted with ether and dried with ignited sodium sulfate. Vacuum distillation yielded 10.1 g (28%) of γ-(ethylmercapto)-propylamine with b.p. 86-87° (23 mm).

n_D^{20} 1.4855, d_{20}^{20} 0.9370, MR 36.48; calc. 36.78.
Found %: N 11.44, 11.52. $C_5H_{13}NS$. Calculated %: N 11.76

γ-Dialkylaminopropylamines

465 g β-dimethylaminopropionitrile (b.p. 169-172°) was dissolved in 500 ml methyl alcohol and saturated with ammonia (40 g) with cooling by a mixture of ice and salt. The mixture was then placed in an autoclave of 2.5 liters capacity and hydrogenated over Raney nickel catalyst (20 g) at 90-100° and a hydrogen pressure of 100-110 atm. The theoretical quantity of hydrogen was absorbed in 2 hours.

Repeated distillation of the product yielded 320 g (68.8%) of γ-dimethylaminopropylamine with b.p. 130-133° [7].

γ-Diethylaminopropylamine with b.p. 168-170° (yield 65%) and γ-(N-piperidyl)-propylamine with b.p. 82-85° at 10 mm (yield 50%) were obtained in the same way.

1-(γ-Dimethylamino)-propyl-2, 5-dimethyl-4-piperidone [I, X=$(CH_3)_2N$]

1) A solution of 13 g of propenyl isopropenyl ketone and its corresponding methoxyketones (b.p. 57-62° at 10 mm; n_D^{20} 1.4520) in 10 ml methyl alcohol was added over a period of 5 minutes to a solution of 10 g γ-dimethylaminopropylamine in 10 ml water. The temperature of the reaction mixture rose to 50°. The mixture was then heated on a water bath at 90° for 8.5 hours, cooled with cold water and acidified to congo red with dilute hydrochloric acid (1 : 1). The methyl alcohol was distilled off in vacuo and the neutral products extracted with ether. The acidified aqueous layer was cooled with ice water, saturated with solid caustic potash and again extracted with three portions of ether. The ether extract was dried with ignited sodium sulfate, the ether distilled off and the product vacuum distilled. This yielded 11 g (64%) of 1-(γ-dimethylamino)-propyl-2, 5-dimethyl-4-piperidone in the form of a colorless liquid:

b.p. 96-97° (2.5 mm), n_D^{20} 1.4726, d_{20}^{20} 0.9369, MR 63.53; calc. 63.33.
Found %: N 12.91, 12.93. $C_{12}H_{24}ON_2$. Calculated %: N 13.19.

The dihydrochloride of this piperidone was prepared by the action of dry hydrogen chloride on an ethereal solution of the base. After two recrystallizations from alcohol it had m.p. 187-188°.

2) A mixture of 18.3 g γ-dimethylaminopropylamine, 29 g propenyl isopropenyl ketone and the corresponding methoxyketones, 18 ml water and 18 ml methyl alcohol was left at room temperature for 6 hours. The mixture was then made weakly acid to congo red with dilute hydrochloric acid (1 : 1) and treated as in the previous experiment.

Yield 33 g (87%) 1-(γ-dimethylamino)-propyl-2, 5-dimethyl-4-piperidone with b.p. 96-99° (2.5 mm), n_D^{20} 1.4728.

3) A mixture of 13 g propenyl isopropenyl ketone and the corresponding methoxyketones, 20 ml anhydrous methyl alcohol and 10 g γ-dimethylaminopropylamine was heated at 90-93° for 8.5 hours and treated as in the previous experiment.

Two distillations of the basic products yielded 4.8 g (28%) 1-(γ-dimethylamino)-propyl-2, 5-dimethyl-4-piperidone with b.p. 94-96° (2 mm), n_D^{20} 1.4728.

5.5 g of unreacted methoxyketones with b.p. 60-62° at 9 mm was recovered from the neutral products in this experiment.

It should be noted that all the 1-(dimethylamino)-propyl-4-piperidones prepared by us have an irritating action on the skin.

1-(γ-Diethylamino)-propyl-2, 5-dimethyl-4 piperidone [I, X=$(C_2H_5)_2N$]

A mixture of 10 g γ-diethylaminopropylamine, 12 g propenyl isopropenyl ketone and the corresponding methoxyketones, 10 ml water and 10 ml methyl alcohol was left at room temperature for 8 hours.

The usual treatment yielded 14.2 g (77%) 1-(γ-diethylamino)-propyl-2, 5-dimethyl-4-piperidone:

b.p. 118-120° (2 mm), n_D^{20} 1.4678, d_{20}^{20} 0.9146, MR 72.98; calc. 72.56.
Found %: N 11.84, 11.79. $C_{14}H_{28}ON_2$. Calculated %: N 11.66

1-(γ-N-Piperidyl)-propyl-2, 5-dimethyl-4-piperidone [I, X=(CH_2) N]

A mixture of 10.2 g γ-(N-piperidyl)-propylamine, 10 g propenyl isopropenyl ketone (b.p. 47-50° at 12 mm, n_D^{20} 1.4680), 10 ml water and 10 ml methyl alcohol was left at room temperature for 24 hours.

The usual treatment yielded 10.5 g (57.5%) of 1-(γ-N-piperidyl)-propyl-2, 5-dimethyl-4-piperidone:

b.p. 126-127° (1 mm), n_D^{20} 1.4885, d_{20}^{20} 0.9717, MR 74.90; calc. 74.96.
Found %: N 11.30, 11.21 $C_{15}H_{28}ON_2$. Calculated %: N 11.10.

1-(γ-Methoxy)-propyl-2, 5-dimethyl-4-piperidone (I, X=CH_3O)

A mixture of 14 g propenyl isopropenyl ketone and the corresponding methoxyketones, 10 g γ-methoxy-propylamine, 10 ml water and 10 ml methyl alcohol was left at room temperature for 4 hours and then heated at 50-55° for 2 hours. The usual treatment yielded 16.7 g (75%) of 1-(γ-methoxy)-propyl-2, 5-dimethyl-4-piperidone:

b.p. 110-111° (3 mm), n_D^{20} 1.4547, d_{20}^{20} 0.9564, MR 56.21; calc. 56.38.
Found %: N 7.20, 7.12. $C_{11}H_{21}O_2N$. Calculated %: N 7.03.

When an ethereal solution of this piperidone was saturated with dry hydrogen chloride, the hydrochloride separated in the form of an oil which crystallized slowly on prolonged standing in ether. After recrystallization from acetone the 1-(γ-methoxy)-propyl-2, 5-dimethyl-4-piperidone hydrochloride melted at 133-134°.

1-(γ-Methoxy) propyl-2, 5-dimethylpiperidine. A mixture of 11 g 1-(γ-methoxy)-propyl-2, 5-dimethyl-4-piperidone (b.p. 105-107° at 3 mm), 17 g hydrazine hydrate, 25 ml ethyl alcohol and 5 ml water was heated for 5 hours at 70-75°. The alcohol was then removed in vacuo, the residue treated with alkali, extracted with ether and dried with fused alkali. After drying, the ether was distilled off, the residue placed in a flask fitted with a reflux condenser and heated for 3 hours at 150-160° with a small quantity of caustic potash fused in a silver crucible (Kizhner catalyst). A vigorous evolution of nitrogen took place from the decomposition of the hydrazone. The residue from the decomposition was extracted with dry ether and vacuum distilled.

Yield—5.5 g (53%) 1-(γ-methoxy)-propyl-2, 5-dimethylpiperidine:

b.p. 60-62° (2.5 mm), n_D^{20} 1.4520, d_{20}^{20} 0.8874, MR 56.35; calc. 56.38.
Found %: N 8.01, 7.92. $C_{11}H_{23}ON$. Calculated %: N 7.56.

1-(γ-Dimethoxy)-propyl-2, 5-dimethylpiperidine hydrochloride was prepared in the usual way. After recrystallization from acetone it melted at 131.5-133°.

1-(γ-Ethoxy)-propyl-2, 5-dimethyl-4-piperidone (I, X=C_2H_5O)

A mixture of 12 g γ-ethoxypropylamine, 18 g propenyl isopropenyl ketone and the corresponding methoxy-ketones, 12 ml water and 15 ml methyl alcohol was left for 3 hours at room temperature and then heated for 2.5 hours at 50°.

The usual treatment yielded 15.2 g (68.7%) of 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4-piperidone:

b.p. 116-118° (2.5 mm), n_D^{20} 1.4554, d_{20}^{20} 0.9468, MR 61.09; calc. 61.00.
Found %: N 6.68, 6.88. $C_{12}H_{23}O_2N$. Calculated %: N 6.57.

Hydrochloride—oily liquid which did not crystallize.

<u>1-(γ-Ethoxy)-propyl-2, 5-dimethylpiperidine.</u> 5.4 g 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4-piperidone (b.p. 98-100° at 1.5 mm, n_D^{20} 1.4554) was mixed with 10 ml hydrazine hydrate, 10 ml ethyl alcohol and 4 ml water. The mixture was heated on a water bath at 70-75° for 5 hours. The alcohol was then distilled off in vacuo and the residue treated with solid alkali. The oil which rose to the surface was extracted with ether and carefully dried with fused alkali. The decomposition of the hydrazone was carried out as in the previous experiment. After distillation, 2.1 g (41.5%) 1-(γ-ethoxy)-propyl-2, 5-dimethylpiperidine was obtained:

b.p. 58-60° (2 mm), n_D^{27} 1.4524, d_{20}^{20} 0.8790, MR 61.20; calc. 61.00.
Found %: N 6.86, 6.74. $C_{12}H_{25}ON$. Calculated %: N 7.03.

Hydrochloride—an oily liquid which did not crystallize.

<u>1-(γ-n-Propoxy)-propyl-2, 5-dimethyl-4-piperidone [I, X= n—C_3H_7O]</u>

A mixture of 12 g γ-n propoxypropylamine, 16 g propenyl isopropenyl ketone and the corresponding methoxyketones, 12 ml water and 15 ml methyl alcohol was left for 3 hours at room temperature and then heated for 2.5 hours at 50-55°.

The usual treatment yielded 15.6 g (67%) of 1-(γ-n-propoxy)-propyl-2, 5-dimethyl-4-piperidone:

b.p. 117-119° (1.5 mm), n_D^{20} 1.4545, d_{20}^{20} 0.9357, MR 65.81; calc. 65.61.
Found %: N 6.40, 6.32. $C_{13}H_{25}O_2N$. Calculated %: N 6.17.

Hydrochloride—an oil which did not crystallize.

<u>1-(γ-n-Butoxy)-propyl-2, 5-dimethyl-4-piperidone [I, X=n-C_4H_9O]</u>

A mixture of 15 g γ-n-butoxypropylamine, 19 g propenyl isopropenyl ketone and its corresponding methoxyketones, 15 ml water and 15 ml methyl alcohol was left to stand for 3 hours at room temperature and then heated for 2.5 hours at 50-55°. The usual treatment yielded 17.9 g (65%) of 1-(γ-n-butoxy)-propyl-2, 5-dimethyl 4-piperidone:

b.p. 127-129° (2 mm), n_D^{20} 1.4494, d_{20}^{20} 0.9171, MR 70.48; calc. 70.25.
Found %: N 6.05, 5.89. $C_{14}H_{27}O_2N$. Calculated %: N 5.81.

Hydrochloride—an oil which did not crystallize.

<u>1-(γ-Ethylmercapto)-propyl-2, 5-dimethyl-4-piperidone [I, X=C_2H_5S]</u>

A mixture of 10 g freshly distilled propenyl isopropenyl ketone (b.p. 62-63° at 24 mm), 8.2 g γ-ethylmercaptopropylamine (b.p. 182-187°), 10 ml methyl alcohol and 8 ml water were left to stand at room temperature for 5.5 hours and then heated for 1.5 hours at 50-60°.

After the usual treatment 10.8 g (68%) of 1-(γ-ethylmercapto)-propyl-2, 5-dimethyl-4-piperidone was obtained:

b.p. 117-118° (1.5 mm), n_D^{20} 1.4915, d_{20}^{20} 0.9896, MR 67.18; calc. 67.43.
Found %: 6.49, 6.37. $C_{12}H_{23}ONS$. Calculated %: N 6.10.

Picrate—an oil which did not crystallize.

<u>1-(γ-Dimethylamino)-propyl-2, 5, 6-trimethyl-4-piperidone [II, X=$(CH_3)_2N$]</u>

A mixture of 10 g γ-dimethylaminopropylamine, 16 g 5-methyl-2, 5-heptadiene-4-one (b.p. 72-75° at 7 mm), 10 ml water and 20 ml methyl alcohol was left to stand at room temperature for 6 hours and then heated for 40 minutes at 50-60°. After the usual treatment the product was vacuum distilled. Yield—15.8 g (72%) of 1-(γ-dimethylamino)-propyl-2, 5, 6-trimethyl-4-piperidone:

b.p. 104-106° (1.5 mm), n_D^{20} 1.4742, d_{20}^{20} 0.9420, MR 67.53; calc. 67.91.
Found %: N 12.54, 12.50. $C_{13}H_{26}ON_2$. Calculated %: N 12.45.

1-(γ-Diethylamino)-propyl-2, 5, 6-trimethyl-4-piperidone [II, X=$(C_2H_5)_2N$]

A mixture of 8 g γ-diethylaminopropylamine, 10 g 5-methyl-2, 5-heptadiene-4-one, 10 ml water and 15 ml methyl alcohol was left for 6 hours at room temperature and then heated for 40 minutes at 50-60°.

After the usual treatment and vacuum distillation, 11.9 g (71.5%) of 1-(γ-diethylamino)-propyl-2, 5, 6-trimethyl-4-piperidone was obtained:

b.p. 112-113° (1.5 mm), n_D^{20} 1.4736, d_{20}^{20} 0.9309, MR 76.67; calc. 77.16.
Found %: N 11.12, 11.30. $C_{15}H_{30}ON_2$. Calculated %: N 11.02.

1-(γ-Methoxy)-propyl-2, 5, 6-trimethyl-4-piperidone [II, X=CH_3O]

A mixture of 10 g γ-methoxypropylamine, 16 g 5-methyl-2, 5-heptadiene-4-one, 10 ml water and 10 ml methyl alcohol was left at room temperauter for 5 hours and then heated for 1 hour at 50-55°.

After the usual treatment and vacuum distillation, 16.9 g (71%) of 1-(γ-methoxy)-propyl-2, 5, 6-trimethyl-4-piperidone was obtained:

b.p. 97-98° (1.5 mm), n_D^{20} 1.4700, d_{20}^{20} 0.9770, MR 60.85; calc. 61.00.
Found %: N 6.83, 6.88. $C_{12}H_{23}O_2N$. Calculated %: N 6.57.

1-(γ-Ethoxy)-propyl-2, 5, 6-trimethyl-4-piperidone [II, X=C_2H_5O]

A mixture of 10 g γ-ethoxypropylamine, 15 g 5-methyl-2, 5-heptadiene-4-one, 10 ml water and 10 ml methyl alcohol was left to stand for 5 hours at room temperature and then heated for 1 hour at 50 55°.

Yield–15.6 g (70%) of 1-(γ-ethoxy)-propyl-2, 5, 6-trimethyl-4-piperidone:

b.p. 110-111° (2 mm), n_D^{20} 1.4672, d_{20}^{20} 0.9633, MR 65.46; calc. 65.61.
Found %: N 6.17, 6.39. $C_{13}H_{25}O_2N$. Calculated %: N 6.17.

1-(γ-n-Propoxy)-propyl-2, 5, 6-trimethyl-4-piperidone [II, X=n-C_3H_7O]

A mixture of 10 g γ-n-propoxypropylamine, 15 g 5-methyl-2, 5-heptadiene-4-one, 10 ml water and 18 ml methyl alcohol was left to stand for 6 hours at room temperature and then heated for 2.5 hours at 50-55°.

Yield–15 g (73%) of 1-(γ-n-propoxy)-propyl-2, 5, 6-trimethyl-4-piperidone:

b.p. 111-112° (1.5 mm), n_D^{20} 1.4645, d_{20}^{20} 0.9510, MR 70.04; calc. 70.24.
Found %: N 5.89, 5.89. $C_{14}H_{27}O_2N$. Calculated %: N 5.81.

1-(γ-n-Butoxy) propyl-2, 5, 6-trimethyl-4-piperidone [II, X=n-C_4H_9O]

A mixture of 10 g γ-n-butoxypropylamine, 15 g 5-methyl-2, 5-heptadiene-4-one, 12 ml water and 20 ml methyl alcohol was left to stand for 6 hours and then heated for 2.5 hours at 50-55°.

Yield–13.6 g (70%) 1-(γ-n-butoxy)-propyl-2, 5, 6-trimethyl-4-piperidone:

b.p. 119-120° (2 mm), n_D^{20} 1.4638, d_{20}^{20} 0.9411, MR 74.80; calc. 74.85.
Found %: N 5.65, 5.73. $C_{15}H_{29}O_2N$. Calculated %: N 5.49.

1-(γ-Dimethylamino) propyl-2-methyl-4-ketodecahydroquinoline [III, X=$(CH_3)_2N$]

A mixture of 20 g γ-dimethylaminopropylamine, 23.2 g propenyl Δ'-cyclohexenyl ketone (b.p. 105-107° at 7 mm), 20 ml water and 25 ml methyl alcohol was left at room temperature for 4 hours and then heated for 30 minutes on the water bath at 50°.

The usual treatment yielded 39 g (80%) of 1-(γ-dimethylamino)-propyl-2-methyl-4-ketodecahydroquinoline:

b.p. 138-140° (2.5 mm), n_D^{20} 1.4958, d_{20}^{20} 0.9884, MR 74.56; calc. 74.85.
Found %: N 11.27, 11.45. $C_{15}H_{26}ON_2$. Calculated %: N 11.10.

1-(γ-Diethylamino)-propyl-2-methyl-4-ketodecahydroquinoline [III, X=$(C_2H_5)_2N$]

A mixture of 8 g γ-diethylaminopropylamine, 11 g propenyl Δ'-cyclohexenyl ketone, 10 ml water and 12 ml methyl alcohol was left at room temperature for 4 hours and then heated for 20 minutes at 50-55°.

The usual treatment yielded 13.8 g (81%) 1-(γ-diethylamino)-propyl-2-methyl-4-ketodecahydroquinoline:

b.p. 146-147° (2 mm), n_D^{20} 1.4925, d_{20}^{20} 0.9719, MR 83.80; calc. 84.19.
Found %: N 10.31, 10.27. $C_{17}H_{30}ON_2$. Calculated %: N 10.00.

1-(γ-N-Piperidyl)-propyl-2 methyl-4-ketodecahydroquinoline [III, X=$(CH_2)_5N$]

A mixture of 10 g γ-(N-piperidyl)-propylamine, 13 g propenyl Δ'-cyclohexenyl ketone, 10 ml water and 13 ml methyl alcohol was left at room temperaute for 3 hours and then heated on the water bath at 60° for 1 hour.

After the usual treatment and vacuum distillation of the product, 13.2 g (64.5%) of 1-(γ-N-piperidyl)-propyl-2-methyl-4-ketodecahydroquinoline was obtained:

b.p. 159-161° (2 mm), n_D^{20} 1.4963, d_{20}^{20} 0.9854, MR 86.73; calc. 86.61.
Found %: N 9.29, 9.67. $C_{18}H_{32}ON_2$. Calculated %: N 9.57.

1-(γ-Methoxy)-propyl-2-methyl-4-ketodecahydroquinoline [III, X=CH_3O]

A mixture of 10 g γ-methoxypropylamine, 18 g propenyl Δ'-cyclohexenyl ketone, 10 ml water and 15 ml methyl alcohol was left at room temperature for 6 hours. The reaction mixture was then acidified to congo red with dilute hydrochloric acid, the methyl alcohol distilled off in vacuo, the neutral products extracted and the solution saturated with alkali. The oil which rose to the surface was extracted several times with ether, dried with ignited sodium sulfate and vacuum distilled.

Yield–22.1 g (82.5%) 1-(γ-methoxy)-propyl-2-methyl-4-ketodecahydroquinoline:

b.p. 134-135° (2.5 mm), n_D^{20} 1.4951, d_{20}^{20} 1.0219, MR 68.42; calc. 68.04.
Found %: N 5.97, 6.00. $C_{14}H_{25}O_2N$. Calculated %: N 5.87.

The picrate was obtained by mixing alcoholic solutions of the base and picric acid. After recrystallization from alcohol it melted at 133-135°.

Found %: N 11.85, 11.59. $C_{20}H_{28}O_9N_4$. Calculated %: N 11.95.

1-(γ-Ethoxy)-propyl-2-methyl-4-ketodecahydroquinoline [III, X=C_2H_5O]

A mixture of 10 g γ-ethoxypropylamine, 17 g propenyl Δ'-cyclohexenyl ketone, 10 ml water and 15 ml methyl alcohol was left for 6 hours at room temperature and then treated as in the previous experiment.

Yield–20 g (81.7%) 1-(γ-ethoxy)-propyl-2-methyl-4-ketodecahydroquinoline:

b.p. 140-142° (2.5 mm), n_D^{20} 1.4880, d_{20}^{20} 1.0075, MR 72.33; calc. 72.66.
Found %: N 5.52, 5.39. $C_{15}H_{25}O_2N$. Calculated %: N 5.52.

1-(γ-Ethoxy)-propyl-2-methyldecahydroquinoline. 15 g hydrazine hydrate, 30 ml ethyl alcohol and 5 ml water were added to 10 g of 1-(γ-ethoxy)-propyl-2-methyl-4-ketodecahydroquinoline (b.p. 140-142° at 2 mm, n_D^{20} 1.4870). The mixture was heated for 5 hours at 75-80°, the alcohol distilled off in vacuo, the residue treated with alkali and the reaction product extracted with ether. The ether extract was carefully dried with fused alkali, the ether distilled off and the hydrazone left was decomposed with Kizhner catalyst at 150-160° for 5 hours. The product was extracted with dry ether and vacuum distilled.

Yield–7.0 g (74%) 1-(γ-ethoxy)-propyl-2-methyldecahydroquinoline:

b.p. 119° (3 mm), n_D^{20} 1.4795, d_{20}^{20} 0.9380, MR 72.41; calc. 72.65.
Found %: N 5.75, 6.15. $C_{15}H_{29}ON$. Calculated %: N 5.85.

The hydrochloride was prepared by the action of hydrogen chloride on an ethereal solution of the base. After two recrystallizations from acetone it melted at 120-122°.

1-(γ-n-Propoxy)-propyl-2-methyl-4-ketodecahydroquinoline [III, X=n-C_3H_7O]

A mixture of 10 g γ-n-propoxypropylamine, 14 g propenyl Δ'-cyclohexenyl ketone, 10 ml water and 15 ml methyl alcohol was left for 5 hours at room temperature and then heated for 30 minutes at 50-55°.

The usual treatment yielded 19 g (83%) of 1-(γ-n-propoxy)-propyl-2-methyl-4-ketodecahydroquinoline:

b.p. 142-143° (2 mm), n_D^{20} 1.4885, d_{20}^{20} 0.9940, MR 77.16; calc. 77.27
Found %: N 5.33, 5.18. $C_{16}H_{17}O_2N$. Calculated %: N 5.24.

1-(γ-n-Butoxy)-propyl-2-methyl-4-ketodecahydroquinoline [III, X=n-C_4H_9O]

A mixture of 10 g γ-butoxypropylamine, 13 g propenyl Δ'-cyclohexenyl ketone, 10 ml water and 15 ml methyl alcohol was left for 5 hours at room temperature and then heated for 30 minutes at 50-55°.

The usual treatment yielded 16.5 g (74.5%) 1-(γ-n-butoxy)-propyl-2-methyl-4-ketodecahydroquinoline:

b.p. 151-152° (2.5 mm), n_D^{20} 1.4856, d_{20}^{20} 0.9856, MR 81.00; calc. 81.91.
Found %: N 4.94, 5.17. $C_{17}H_{19}O_2N$. Calculated %: N 5.00.

SUMMARY

1-γ-alkoxypropyl-4-piperidones, 1-γ-alkylmercaptopropyl-4-piperidones and 1-γ-dialkylaminopropyl-4-piperidones have been prepared in good yield (70-90%) by the action of γ-alkoxypropylamines, γ-alkylmercaptopropylamines and γ-dialkylaminopropylamines on vinyl propenyl ketones or the corresponding β-methoxyketones formed as the result of the addition of methanol to the vinyl propenyl ketones.

The above reaction with β-methoxyketones takes place readily only in the presence of water. In this way more than twenty γ-piperidones and 2-methyldecahydroquinolines containing γ-alkoxypropyl, γ-alkylmercaptopropyl and γ-dialkylaminopropyl radicals on the nitrogen atom have been prepared for the first time.

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* T. p. = C. B. Translation pagination.

HETEROCYCLIC COMPOUNDS

53. SYNTHETIC PAIN-RELIEVING MATERIALS

XV. THE SYNTHESIS OF 2, 5-DIMETHYL-4-PHENYL-4-PIPERIDOLS AND THEIR ESTERS, CONTAINING γ-SUBSTITUTED PROPYL RADICALS ON THE NITROGEN. ANALOGS OF PROMEDOL AND ISOPROMEDOL. II.

I. N. Nazarov and S. M. Makin

In an earlier communication we described the synthesis of γ-piperidones and decahydroquinolines with γ-alkoxypropyl, γ-alkylmercaptopropyl and γ-dialkylaminopropyl substituents on the nitrogen of the piperidine nucleus [1]:

$X = OCH_3$; OC_2H_5; OC_3H_7-n.; OC_4H_9-n. SC_2H_5; $N(CH_3)_2$; $N(C_2H_5)_2$; N⟨ ⟩

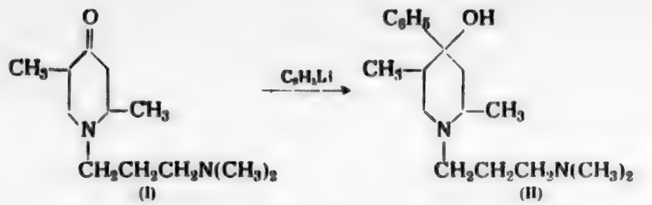
We have now used certain of these γ-piperidones for the synthesis of 4-phenyl-4-piperidols and their esters (acetates and propionates), which belong, as is known, to a class of highly active pain-relieving materials.

Up to the present time extensive research has been carried out in our laboratory [2] and also by several authors in other countries [3] on the synthesis of esters of 4-phenyl 4-piperidols with different alkyl substituents on the nitrogen of the piperidine nucleus, with the aim of finding the influence of these substituents on the physiological (pain-relieving) activity of these esters.

Considerable interest has also been attached to the preparation of esters of 4-phenyl-4-piperidols containing different functional groups in the alkyl radicals attached to the nitrogen of the piperidine nucleus, with the aim of establishing the influence of these groups on the physiological (pain-relieving) activity of these esters.

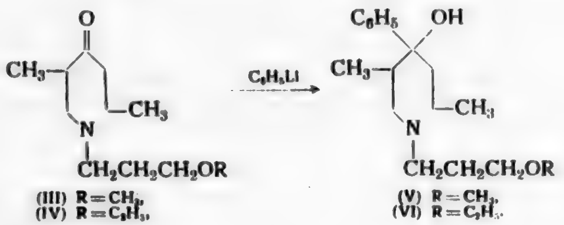
1-(γ-Dimethylamino)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (II) was prepared by the action of phenyllithium on 1-(γ-dimethylamino)-propyl-2, 5-dimethyl-4-piperidone (I).

After vacuum distillation the piperidol (II) was obtained in the form of a very thick liquid with a light yellow color. This alcohol contains 3 asymmetric carbon atoms in the molecule, so that four diastereoisomeric forms are theoretically possible. Repeated attempts to recrystallize this piperidol in different ways and isolate the different stereoisomeric forms by fractional crystallization, however, have not led to the desired results. When dry hydrogen chloride was passed through an ethereal solution of this amino alcohol, an amorphous precipitate of the dihydrochloride was obtained, which rapidly absorbed moisture from the atmosphere. The dihydrochloride could be partly crystallized with great difficulty only after repeated precipitation from alcoholic solution with dry ether.

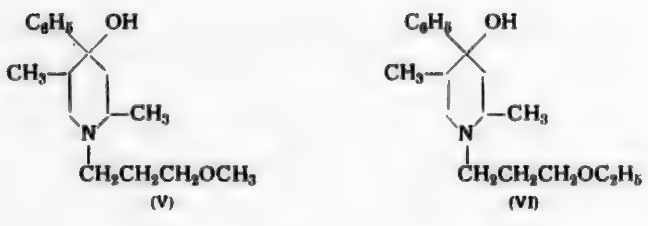


We have thus been unable to separate 1-(γ-dimethylamino)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (II) into stereoisomeric forms.

1-(γ-Methoxy)- and 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidols (V) and (VI) were prepared by the action of phenyllithium on 1-(γ-methoxy)- and 1-(γ-ethoxy) propyl-2, 5-dimethyl-4-piperidones (III) and (IV).



Two sterolsomeric forms (from the four theoretically possible) of these piperidols have been isolated in each case by repeated crystallization first in the form of the bases and then in the form of the hydrochlorides.

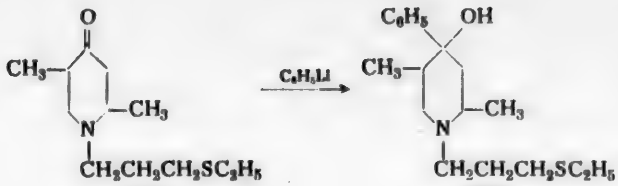


α-Form, m.p. 69-70°; hydrochloride, m.p. 197-198°.
β-Form, liquid; hydrochloride, m.p. 149-150°.

α-Form, m.p. 63-64°; hydrochloride, m.p. 191-192.5°.
β-Form, liquid; hydrochloride, m.p. 148-149°.

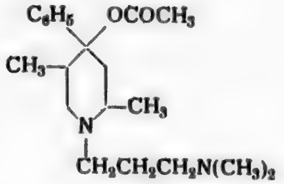
1-(γ-Ethylmercapto)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (VIII), whose free base is an oily liquid which does not crystallize, was prepared similarly by the action of phenyllithium on 1-(γ-ethylmercapto)-propyl-2, 5-dimethyl 4-piperidone (VII). The hydrochloride of this piperidol forms hygroscopic crystals and was partly crystallized from a mixture of alcohol and acetone.

The acetates and propionates (IX) and (X) of 1-(γ-dimethylamino)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (II) were synthesized by heating the hydrochloride of piperidol (II) with acetyl or propionyl chloride in a

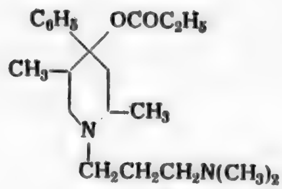


(VII) (VIII)

medium of the corresponding anhydrides. This method is convenient, since after vacuum distillation of the excess anhydride, the hydrochloride of the ester is left in a readily crystallizable form, and can be obtained in a pure state after one or two recrystallizations.

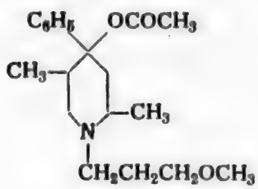


(IX)

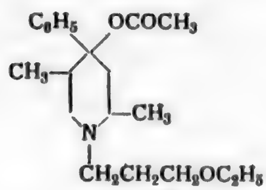


(X)

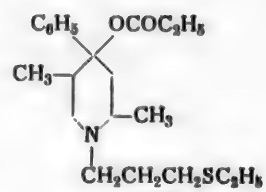
The acetates of the high-melting isomers of 1-(γ-methoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (XI) and 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (XII), and the propionate of 1-(γ-ethylmercapto)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (XIII) were prepared in the same way:



(XI)

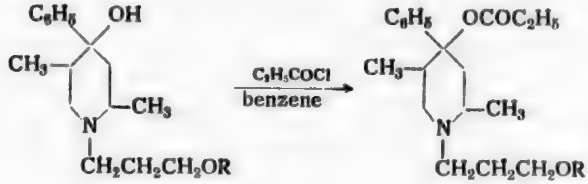


(XII)



(XIII)

The propionates of the high-melting isomers of 1-(γ-methoxy)- and 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidols (XIV) and (XV) were prepared by the action of propionyl chloride on piperidols (V) and (VI) in dry benzene in the presence of metallic magnesium (Spasov's method [4]).



R = CH_3 (XIV),
R = C_2H_5 (XV).

Results of Pharmacological Tests

1-(γ-Methoxy)- and 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl propionates (XIV) and (XV) exhibit a powerful pain-relieving action, as great as that of morphine. At the same time these esters show a pronounced local anesthetic action, which is several times greater than that of novocaine.

Their anesthetizing action is approximately half that of dicaine, but they are considerably less toxic than the latter. It should be noted that such a combination of powerful pain-relieving and local anesthetic action in the one compound is met with extremely rarely and is an interesting peculiarity of these compounds.

1-(γ-Methoxy)- and 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl acetates (XI) and (XII) have a slightly lower pain-relieving activity than that of morphine, while the esters of 1-(γ-dimethylamino)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (IX) and (X) have practically no pain-relieving activity.

The analgesic activity of all the esters described in the present communication is still, however, considerably lower than the activity of promedol* and isopromedol. Thus in comparison with the other known substituents, the methyl radical on the nitrogen atom exerts the most favorable influence on the analgesic activity of the esters of 4-phenyl-4-piperidols.

The pharmacological studies were carried out in the pharmacology section of the S. Ordzhonikidze All-Union Chemical and Pharmaceutical Scientific Research Institute under the direction of M. D. Mashkovsky.

EXPERIMENTAL

1-(γ-Dimethylamino)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (II)

57 g of 1-(γ-dimethylamino)-propyl-2, 5-dimethyl-4-piperidone (I) (b.p. 96-97° at 2.5 mm, n_D^{20} 1.4726) was added dropwise over a period of 2.5 hours with cooling by a mixture of ice and salt to the ethereal solution of phenyllithium prepared in the usual way in an atmosphere of nitrogen from 57 g bromobenzene, 5.7 g lithium and 100 ml absolute ether. When all the piperidone had been added, the reaction mixture was stirred for 5 hours at room temperature and left overnight. The next day stirring was continued for a further 2 hours with the ether boiling. The flask was cooled with ice water and the reaction mass acidified to congo red with dilute hydrochloric acid (1:1). The ether layer was removed, the aqueous layer washed with ether and treated with solid alkali. The oil which rose to the surface was extracted with ether and dried with ignited sodium sulfate.

Vacuum distillation of the product yielded 17.5 g of the original piperidone (I) (b.p. 95-100° at 2 mm) and 43.6 g (56%) of 1-(γ-dimethylamino)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (II) with b.p. 160-162° (1.5 mm).

Found %: 9.66, 9.48. $C_{18}H_{30}ON_2$. Calculated %: N 9.66.

Repeated attempts to separate this piperidol into isomers, either in the form of the free bases or in the form of the dihydrochlorides or picrates, gave no positive results.

The dihydrochloride of this piperidol was obtained by the action of hydrogen chloride on an ethereal solution of the base and had the form of very fine snow-white crystals with m.p. 223-224°.

Found %: N 8.04, 7.67. $C_{18}H_{32}O_2N_2Cl_2$. Calculated %: N 7.70.

1-(γ-Methoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (V)

The reaction was carried out in a three-necked flask of 500 ml capacity fitted with mechanical stirrer, reflux condenser, dropping funnel, thermometer and tube for nitrogen, which was passed through for the duration of the experiment. 60 ml absolute ether and 4.5 g finely divided metallic lithium were placed in the flask and 47 g bromobenzene in 80 ml absolute ether added dropwise over a period of 4 hours. A further 120 ml absolute ether was added to the mixture and the reaction mass heated for 2 hours at the boiling point of the ether. When reaction was complete the flask and the prepared phenyllithium were cooled to minus 15° and a solution of 38 g 1-(γ-methoxy)-propyl-2, 5-dimethyl-4-piperidone (III) (b.p. 105-107° at 3 mm, n_D^{20} 1.4547) in 40 ml absolute ether added dropwise with stirring over a period of 4 hours.

The next day the contents of the flask were stirred for 4 hours at room temperature and then for a further 2 hours at the boiling point of the ether. The alkoxide obtained was hydrolyzed by the addition of 100 ml of ice

*Russian trade name.

water. The ether layer was removed, the aqueous layer saturated with alkali and extracted several times with ether. The combined ether extracts were dried with sodium sulfate. Vacuum distillation of the product yielded 10 g of the original piperidone (III) (b.p. 100-105° at 2 mm) and 23 g 1-(γ-methoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (V) in the form of a thick yellowish liquid with b.p. 155-158° (1 mm), which partly crystallized on the addition of benzene and cooling. The crystals were pressed out at the water pump and recrystallized from benzene to yield 8.1 g of the α-form of 1-(γ-methoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol with m.p. 69-70°.

Found %: N 5.33, 5.03. $C_{17}H_{27}O_2N$. Calculated %: N 5.05.

The hydrochloride of the α-form was prepared by saturating an ethereal solution of the base (m.p. 69-70°) with dry hydrogen chloride and melted at 197-198° (from a mixture of alcohol and acetone).

The mixture of isomeric piperidols (V) which did not crystallize was converted to the hydrochlorides, which were fractionally crystallized from acetone. In this way a further quantity (1.2 g) of the hydrochloride of the α-form with m.p. 197-198° was obtained, together with 1.3 g of the hydrochloride of the β-form of piperidol (V) with m.p. 149-150° in the form of large colorless plates.

Found %: N 4.51, 4.64. $C_{17}H_{28}O_2NCl$. Calculated %: N 4.47.

The free base of the β-form of 1-(γ-methoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol, obtained from the hydrochloride with m.p. 148-149° by treatment with aqueous ammonia, was a noncrystallizable thick liquid with b.p. 159-160° (1.5 mm).

Found %: C 73.27, 73.37; H 10.01, 10.13. $C_{17}H_{27}O_2N$. Calculated %: C 73.61; H 9.87.

1-(γ-Ethoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (VI)

50 g 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4-piperidone (IV) (b.p. 116-118° at 2 mm, n_D^{20} 1.4554) was added dropwise over a period of 2 hours with cooling by a mixture of ice and salt to an ethereal solution of phenyllithium prepared as in the previous experiment from 48 g bromobenzene, 4.7 g lithium and 120 ml absolute ether. The reaction mass was stirred for 1 hour at room temperature and for 3 hours at the boiling point of the ether, and then treated with 18% hydrochloric acid until acid to congo red (140 ml) with cooling by ice water. The ether layer was removed, the aqueous layer saturated with solid caustic soda and extracted with ether. The ether extract was dried with sodium sulfate and the residue after removal of the ether vacuum distilled: 1st fraction, b.p. 95-100° (2 mm), 12 g; 2nd fraction, b.p. 160-165° (2 mm), 36 g; nonvolatile residue—6 g.

The second fraction, a mixture of the isomeric 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4 phenyl-4-piperidols (VI), partly crystallized on the addition of benzene and cooling. Two recrystallizations from benzene yielded 14.8 g of crystals of an individual isomer with m.p. 63-64° (α-form).

Found %: N 5.38, 5.25. $C_{18}H_{29}O_2N$. Calculated %: N 4.80.

The hydrochloride of this isomer was obtained by saturating an ethereal solution of the base (m.p. 63-64°) with dry hydrogen chloride. After two recrystallizations from a mixture of alcohol and acetone it melted at 191-192°.

Found %: N 4.55, 4.49. $C_{18}H_{30}O_2NCl$. Calculated %: N 4.27.

The mixture of isomeric piperidols which did not crystallize was converted to the hydrochlorides, which were fractionally crystallized from acetone; this yielded a further 1.8 g of the hydrochloride of the α-isomer with m.p. 191-192° and 2.1 g of the hydrochloride of the β-isomer with m.p. 148-149°.

Found %: N 4.54, 4.54. $C_{18}H_{30}O_2NCl$. Calculated %: N 4.27.

The hydrochloride of the β-isomer with m.p. 148-149° was converted to the base which was then vacuum distilled. The free base of this isomer was a thick liquid with b.p. 160-162° (2 mm).

Found %: N 5.02, 5.18. $C_{18}H_{29}O_2N$. Calculated %: N 4.80.

1-(γ-Ethylmercapto)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (VIII)

10.3 g 1-(γ-ethylmercapto)-propyl-2, 5-dimethyl-4-piperidone (VI) (b.p. 117-118° at 1.5 mm, n_D^{20} 1.4915) in 10 ml absolute ether was added dropwise at room temperature over a period of 40 minutes to an ethereal solution of phenyllithium prepared from 9 g bromobenzene, 1.0 g lithium and 35 ml absolute ether. The reaction mass was heated for 1 hour at the boiling point of the ether and left overnight. The next day the product was treated as described above.

This yielded 2.9 g of the original 1-(γ-ethylmercapto)-propyl-2, 5-dimethyl-4-piperidone with b.p. 127-135° (2.5 mm) and 6.4 g 1-(γ-ethylmercapto)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (VIII) with b.p. 178-180° (2.5 mm) in the form of a very thick light yellow oil.

Found %: N 4.52, 4.61. $C_{18}H_{29}ONS$. Calculated %: N 4.47.

All attempts to crystallize this piperidol by cooling or by the addition of a small quantity of solvent did not lead to the desired result.

The hydrochloride of 1-(γ-ethylmercapto)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol was prepared in the usual way and melted at 164-165° (from a mixture of acetone and alcohol).

Found %: N 4.07, 4.39. $C_{18}H_{30}ONSCl$. Calculated %: N 4.08.

1-(γ-Dimethylamino)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl acetate (IX)

A mixture of 5 g of the dihydrochloride of 1-(γ-dimethylamino)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (II) (m.p. 223-224°), 10 ml acetyl chloride and 20 ml acetic anhydride was heated at 90-100° for 3.5 hours. The precipitate obtained was filtered off, washed with absolute ether and dried in a vacuum desiccator. After recrystallization from a mixture of alcohol and acetone, the 1-(γ-dimethylamino)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl acetate dihydrochloride obtained melted at 231-232°. Yield 3.1 g.

Found %: C 59.33, 59.42, 59.14; H 8.15; 8.63, 8.31; N 6.76, 6.87. $C_{20}H_{34}O_2N_2Cl_2$.
Calculated %: C 59.25; H 8.45; N 6.97.

1-(γ-Dimethylamino)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl propionate (X)

10 g of the dihydrochloride of 1-(γ-dimethylamino)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (II) (m.p. 223-224°), 12 ml propionyl chloride and 30 ml propionic anhydride were placed in a round-bottomed flask fitted with reflux condenser and calcium chloride tube. The reaction mixture was heated for 45 minutes at 100-110° and the dihydrochloride of piperidol (II) dissolved completely. One hour after the dihydrochloride of piperidol (II) had dissolved, a copious precipitate of the dihydrochloride of 1-(γ-dimethylamino)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl propionate (X) was obtained. The heating at 100-110° was continued for a total of 7 hours. The dihydrochloride of the propionate (X) was filtered off, washed with acetone and after three recrystallizations from alcohol melted at 239-240°. Yield 7.5 g. It had the form of very fine snow-white crystals, soluble with difficulty in acetone and anhydrous alcohol.

Found %: N 6.07, 6.02. $C_{21}H_{36}O_2N_2Cl_2$. Calculated %: N 6.67.

1-(γ-Methoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl acetate (XI)

3 g of the hydrochloride of 1-(γ-methoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (V) (m.p. 197-198°), 7 ml acetyl chloride and 20 ml acetic anhydride were mixed in a round-bottomed flask fitted with reflux condenser and calcium chloride tube. The mixture was heated at 100-110° for 10 hours. The acetyl chloride and acetic anhydride were then distilled off in vacuo, the crystalline residue washed with absolute ether and recrystallized twice from acetone. This yielded 3.1 g of the hydrochloride of 1-(γ-methoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl acetate (XI) in the form of snow-white needles with m.p. 177-179°.

Found %: N 3.85, 3.93. $C_{19}H_{30}O_3NCl$. Calculated %: N 3.94.

1-(γ-Methoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl propionate (XIV)

5.0 g 1-(γ-methoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (V) (m.p. 69-70°), 10 ml anhydrous benzene, 10 ml propionyl chloride and 0.2 g magnesium shavings were placed in a three-necked flask of 50 ml

capacity fitted with a mechanical stirrer, thermometer and reflux condenser with calcium chloride tube. The reaction mixture was heated at 80-90° for 9 hours until the precipitate initially formed had disappeared. The excess propionyl chloride and benzene were then distilled off in vacuo at 50°, the thick residue dissolved in 10 ml water, treated with sodium carbonate and extracted with ether. The ether extract was dried with sodium sulfate and vacuum distilled. This yielded 4.7 g of 1-(γ-methoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl propionate (XIV) with b.p. 160-163° (2 mm) in the form of a pale yellowish mobile oil, which was converted into the hydrochloride by saturating its ethereal solution with dry hydrogen chloride. This yielded 4.5 g of the hydrochloride, which after two recrystallizations from acetone melted at 193-194°.

Found %: Cl 9.71, 9.34. $C_{20}H_{32}O_3NCl$. Calculated %: Cl 9.58.

A mixture of this material with the hydrochloride of the original alcohol (m.p. 197-198°) melted at 164-168°.

1-(γ-Ethoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl acetate (XII)

A mixture of 3.5 g of the hydrochloride of 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (VI) (m.p. 191-192.5°), 7 ml acetyl chloride and 20 ml acetic anhydride was heated at 100-110° for 8 hours. The excess acetyl chloride and acetic anhydride were then distilled off in vacuo, the residue which had crystallized was washed with absolute ether and recrystallized twice from a mixture of alcohol and acetone. This yielded 3.5 g of the hydrochloride of 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl acetate (XII) in the form of snow-white needles with m.p. 201-202°.

Found %: C 65.23, 65.25; H 8.61, 8.55; Cl 9.79, 9.72. $C_{20}H_{32}O_3NCl$. Calculated %: C 64.93; H 8.72; Cl 9.58.

A mixture of this compound with the hydrochloride of the original alcohol melted at 161-170°.

1-(γ-Ethoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl propionate (XV)

A mixture of 5 g 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (VI) (m.p. 63-64.5°), 10 ml propionyl chloride, 10 ml anhydrous benzene and 0.2 g magnesium shavings was stirred vigorously at 95-100° for 10 hours until the precipitate initially obtained had dissolved. When the heating was complete the excess propionyl chloride and benzene were distilled off in vacuo, the residue dissolved in 10 ml water, treated with potassium carbonate and extracted with ether. The ether extract was dried with sodium sulfate. The product was vacuum distilled to yield 4.4 g of substance with b.p. 180-182° (3 mm), which was converted to the hydrochloride by saturating its ethereal solution with dry hydrogen chloride. The hydrochloride of 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl propionate (XV) obtained melted at 192-193.5° after three recrystallizations from acetone. Weight 4.1 g.

Found %: Cl 9.20, 9.25. $C_{21}H_{34}O_3NCl$. Calculated %: Cl 9.23.

A mixture of this substance with the hydrochloride of the original alcohol (m.p. 191-192.5°) melted at 165-170°.

1-(γ-Ethylmercapto)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl propionate (XIII)

A solution of 3.5 g of the hydrochloride of 1-(γ-ethylmercapto)-propyl-2, 5-dimethyl-4-phenyl-4-piperidol (VIII) (m.p. 164-165°) and 1.8 ml propionyl chloride in 10 ml propionic anhydride was heated for 8 hours at 100°. The excess propionyl chloride and propionic anhydride were removed, the crystals obtained filtered off and recrystallized from acetone. This yielded 0.5 g of the hydrochloride of 1-(γ-ethylmercapto)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl propionate (XIII), which melted at 173.5-174°.

Found %: N 3.42, 3.71. $C_{21}H_{34}O_2NCl$. Calculated %: N 3.50.

A mixture of this substance with the hydrochloride of the original alcohol melted at 148.5-151°.

The mother solution from the separation of the hydrochloride with m.p. 173.5-174° was evaporated in vacuo, the residue dissolved in water and treated with potassium carbonate. The oil which rose to the surface was extracted with ether, dried with sodium sulfate and vacuum distilled. This yielded 1.4 g of 1-(γ-ethylmercapto)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl propionate (XIII) with b.p. 165-168° (1 mm).

SUMMARY

A number of 1-propyl-2, 5-dimethyl-4-phenyl-4-piperidols and their esters, containing alkoxy, alkysulfido and dialkylamino groups in the propyl radical attached to the nitrogen (in the γ-position) have been synthesized.

1-(γ-Methoxy)- and 1-(γ-ethoxy)-propyl-2, 5-dimethyl-4-phenyl-4-piperidyl propionates combine a high pain-relieving (analgesic) and local anesthetic activity. The analgesic activity of all these compounds, however, is lower than that of promedol.

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*Original Russian pagination. See C. B. Translation.

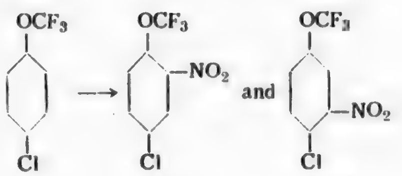
CYANINE DYES CONTAINING FLUORINE

V. THE SYNTHESIS OF CYANINE DYES FROM 5- AND 6-TRIFLUOROMETHOXYBENZOTHIAZOLES

L. M. Yagupolsky and V. I. Troitskaya

The synthesis was recently described by one of us [1] of aromatic compounds containing the OCF_3-group as substituent. Since we have been engaged in a study of the problem of the influence of substituents containing fluorine on the color and efficiency of photo-sensitizing agents, we decided to synthesize 2-methyl-5- and 2-methyl-6-trifluoromethoxybenzothiazoles and to prepare a number of thiacarbocyanines from these bases.

The synthesis of 2-methyl-5-trifluoromethoxybenzothiazole was achieved as follows. 4-Chlorophenyl trifluoromethyl ether (I) was taken as the starting material. This was nitrated to give, apparently, both the isomers (1) and (2):



(I) (1) (2)

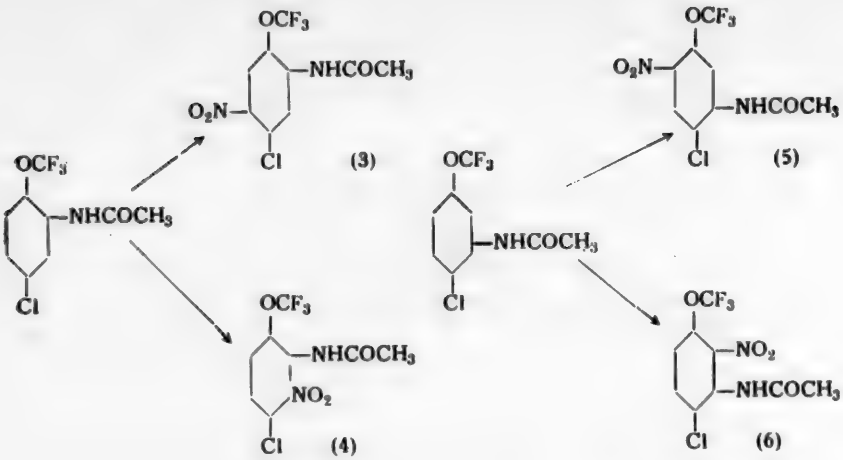
An attempt to hydrolyze the OCF_3-group in these compounds by heating with 50% hydrobromic acid at 150° in a sealed tube was unsuccessful—the substance was unchanged. When an alcoholic solution of the mixture of nitrochloro compounds (1) and (2) obtained was boiled with an alcoholic solution of sodium disulfide, the disulfide was formed, but in very low yield. This fact indicates that the main product of the nitration of 4-chlorophenyl trifluoromethyl ether is the isomer (1).

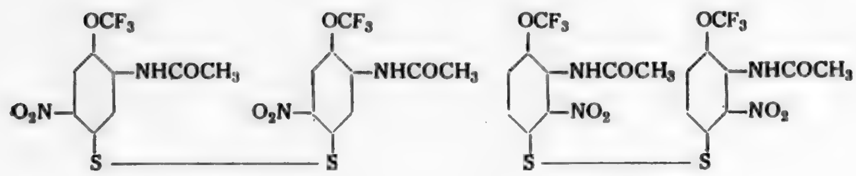
The mixture of nitro isomers was reduced and acetylated. The acetylamino compounds were nitrated further without separation. The formation of four isomers is possible (3, 4, 5 and 6).

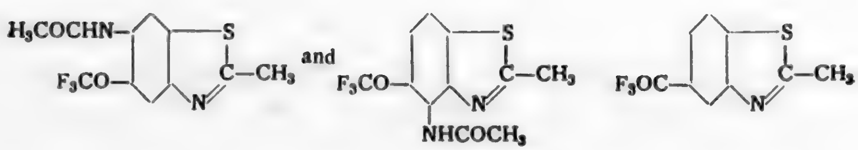
The compounds obtained were heated with an alcoholic solution of sodium disulfide. The isomers (5) and (6) have no mobile halogen atom, so that only the compounds (3) and (4) can react with sodium disulfide, with the formation of two isomeric disulfides.

The mixture of disulfides was reduced with zinc dust to the corresponding aminothiophenols which were converted using acetic anhydride to a mixture of the benzothiazole derivatives (7) and (8).

2-Methyl-5-trifluoromethoxybenzothiazole (9) was obtained from (7) and (8) by hydrolysis of the acetyl group and deamination.



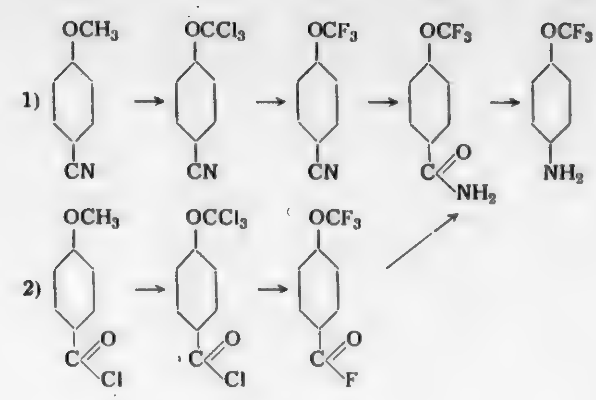


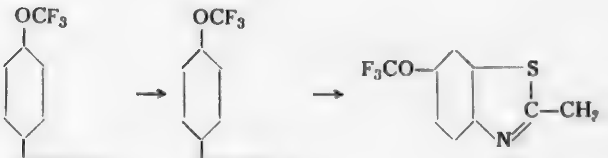


(7) (8) (9)

For the synthesis of 2-methyl-6-trifluoromethoxybenzothiazole we required 4-aminophenyl trifluoromethyl ether. The latter was prepared from the nitrile or chloride of anisic acid.

The second route (starting from the chloride) gives a much bigger yield of amine than the first. The 4-aminophenyl trifluoromethyl ether was acetylated, converted to the thioacetyl derivative and oxidized to 2-methyl-6-trifluoromethoxybenzothiazole (10).





(10)

The bases obtained – 2-methyl-5- and 2-methyl-6-trifluoromethoxybenzothiazoles – were converted to the quaternary salts, from which the thiacarbocyanine, mesomethyl- and mesoethylthiacarbocyanine and styryl dyes were prepared. The structural formulae and absorption maxima of the synthesized cyanine dyes in ethyl alcohol solution are given in the Table; the absorption maxima of the corresponding dyes containing no OCF_3-group are also given for comparison.

It can be seen from the data in the Table that the absorption maxima for the thiacarboxyanines with the OCF_3 substituent group are practically the same as for the unsubstituted dyes (with the exception of the styryls).

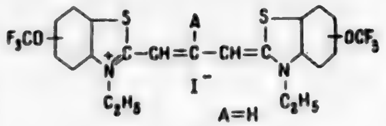
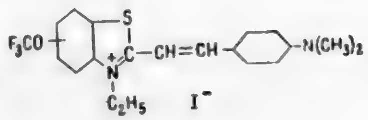
EXPERIMENTAL

4-Chloroanisole was prepared from p-anisidine by replacing the amino group by chlorine by the Sandmeyer reaction (similarly to the preparation of p-chlorotoluene from p-toluidine [2]). Yield 84%, b.p. 195-197°. (Literature data, b.p. 194-198°, uncorrected [3]).

Nitro-4-chlorophenyl trifluoromethyl ether. A nitrating mixture [220 g nitric acid (d 1.5) and 490 g sulfuric acid (d 1.84)] was placed in a three-necked flask fitted with mechanical stirrer, thermomether and dropping funnel, the mixture cooled to 0° and 295 g p-chlorophenyl trifluoromethyl ether (b.p. 140-142°) [1] added dropwise over a period of 1 hour. The mixture was kept at 0° for 30 minutes, for 1 hour at room temperature and for 1.5 hours at 40-50°, cooled and poured on to ice. The product was extracted with ether. The ether solution was washed with water and dried. The ether was removed and the product vacuum distilled. The fraction at 96-99° (7 mm) was collected. Yield 304.2 g (90%).

Found %: N 5.68, 5.80. $C_7H_3O_3NClF_3$. Calculated %: N 5.71.

Amino-4-chlorophenyl trifluoromethyl ether. 250 g iron filings and 300 ml water were placed in a two-liter reaction vessel fitted with mechanical stirrer, reflux condenser, thermometer and dropping funnel and heated to 95°; 20 ml HCl (d 1.19) was added with stirring, the mixture boiled for 10 minutes and 241.5 g nitro-4-chlorophenyl trifluoromethyl ether added from the dropping funnel over a period of 2 hours. The temperature of the

Dye No.	Dye formula	λ_{max}, (in mμ)		
		dyes with OCF3-group in the 6,6' poxitions	dyes with OCF3-group in the 5,5' positions	dyes with no OCF3-group
I II		560	561	558
III IV	To the same A= CH_3	545	548	544
V VI	To the same A= C_2H_5	550	550	550
VII VIII		540	545	530

reaction mixture was kept at 95-98°. When the addition was complete, the mixture was stirred for a further 3 hours at the same temperature. A solution of sodium carbonate was added until the mixture was alkaline and the amine was steam distilled. The amine was extracted from the distillate with ether, the ether solution dried, the ether distilled off and the amine vacuum distilled. The fraction at 76-79° (5 mm) was collected. Yield 182 g (86%).

Found %: N 6.72, 6.75. $C_7H_5ONClF_3$. Calculated %: N 6.62.

Acetylamino-4-chlorophenyl trifluoromethyl ether. A mixture of 53 g amino-4-chlorophenyl trifluoromethyl ether and 31 g acetic anhydride was heated for 15 minutes on the water bath, boiled for 5 minutes, cooled and poured into water. The precipitate was filtered off and recrystallized from aqueous alcohol. Yield 54 g (85%). M.p. 60-65° (melting not sharp).

Found %: N 5.42, 5.54. $C_9H_7O_2NClF_3$. Calculated %: N 5.52.

Nitro-acetylamino-4-chlorophenyl trifluoromethyl ether. 12.7 g acetylamino-4-chlorophenyl trifluoromethyl ether was dissolved with stirring in 20 ml H_2SO_4 (d 1.84) in a three-necked reaction vessel fitted with mechanical stirrer, dropping funnel and thermometer; the solution was cooled to −5° and nitrating mixture (2.7 ml H_2SO_4 d 1.84 and 3.3 ml HNO_3 d 1.41) added dropwise over a period of 15 minutes. The temperature was kept between −5 and 0°. The mixture was then kept at room temperature for 1.5 hours, poured on to ice, the precipitate filtered off, washed with water on the filter and dried. Crystallized from benzene. Yield 7.1 g. M.p. 109-110° (after two crystallizations from benzene).

Found %: N 9.55, 9.61. $C_9H_6O_4N_2ClF_3$. Calculated %: N 9.38.

Diacetylamino-2, 2'-dinitro-4, 4'-bis-trifluoromethoxydiphenyl-1, 1'-disulfide. 5.46 g $Na_2S \cdot 9H_2O$ was dissolved in 30 ml alcohol in a round-bottomed flask with reflux condenser, 0.74 g sulfur added to the solution and the mixture boiled for 30 minutes. The solution obtained was added dropwise over a period of 1 hour to a solution of 13.7 nitro-acetylamino-4-chlorophenyl trifluoromethyl ether in 100 ml alcohol. The mixture was boiled on the water bath for 6 hours. It was then cooled, the precipitate filtered off and washed with water and alcohol. Crystallized from acetic acid. Yield 8.77 g (65%). M.p. 254-255°.

Found %: N 11.07. 11.12. $C_{18}H_{12}O_8N_4S_2F_6$. Calculated %: N 10.84.

Acetylamino-5-trifluoromethoxy-2-methylbenzothiazole. A mixture of 8.8 g diacetylamino-2, 2'-dinitro-4-, 4'-bis-trifluoromethoxydiphenyl-1, 1'-disulfide and 11.5 g zinc dust was added gradually with stirring to 80 ml glacial acetic acid heated to 90-100°, the mixture heated for 15 minutes on a boiling water bath, 23 ml acetic anhydride added and the mixture heated to 120° for 2 hours. It was then cooled to 70-80°, 50 ml water added, the mixture heated to boiling, the precipitate filtered off and washed with 50 ml 50% acetic acid. The mother solution was diluted with 140 ml water and made alkaline with 30% caustic soda. The precipitate was filtered off and washed with alkali and water. Crystallized from ethyl alcohol with charcoal. Yield 4.3 g (50%). M.p. 205-206°. The melting point did not change on subsequent recrystallization.

Found %: N 9.57, 9.62. $C_{11}H_9O_2N_2SF_3$. Calculated %: N 9.65.

Amino-5-trifluoromethoxy-2-methylbenzothiazole. 2 g acetylamino-5-trifluoromethoxy-2-methylbenzothiazole was boiled in a flask with reflux condenser with 20 ml 20% hydrochloric acid for 1 hour, activated charcoal added and boiling continued for a further 5 minutes. The solution was filtered, the amine precipitated with ammonia, filtered off and washed with water. M.p. 94-95° after crystallization from aqueous alcohol. Yield 1.7 g (98%).

Found %: N 11.36, 11.48. $C_9H_7ON_2SF_3$. Calculated %: N 11.29.

2-Methyl-5-trifluoromethoxybenzothiazole. 2.9 g amino-5-trifluoromethoxy-2-methylbenzothiazole was dissolved in 10 ml hydrochloric acid (d 1.19) and 4 ml water in a beaker, the solution cooled to 0° and diazotized with a cooled solution of 0.9 g sodium nitrite in 3 ml water with stirring. When the diazotization was complete, 16 ml of cooled hypophosphorous acid (50% solution) was added gradually and the mixture left overnight. The mixture was diluted with water, made alkaline with ammonia, the precipitate obtained filtered off, washed with water and dried. To purify the specimen, it was dissolved in hydrochloric acid, boiled with charcoal and reprecipitated with ammonia. The product sublimes readily. Yield 2 g (73%).

Found %: N 5.91, 6.01. $C_9H_6ONSF_3$. Calculated %: N 6.00.

The nitrile of anisic acid was prepared by replacing the amino group in p-anisidine by the cyano group by the Sandmeyer reaction (by analogy with the preparation of the nitrile of p-toluic acid from p-toluidine [4]). Yield 50%. B.p. 134-135° (17 mm). M.p. 58-59°. Literature data, m.p. 59.5-60.6° [5].

4-Cyanophenyl trichloromethyl ether. 60 g of the nitrile of anisic acid was mixed with 4.7 g PCl_5 in a small reaction vessel fitted with a bubbler for the passage of chlorine, thermometer and reflux condenser. The mixture was heated to 195° and chlorine passed through for 3.5 hours at 195-200°. Yield of product, assuming that only 4-cyanophenyl trichloromethyl ether is formed, 92 g (87%). The product was fractionated in vacuo and two fractions collected: 1st up to 140° (6 mm), 5 g; 2nd 142-146° (6 mm), 53 g (50%).

The 2nd fraction was distilled a second time for analysis. Material with b.p. 140-141° (5 mm) was collected.

Found %: Cl 44.44, 44.34. $C_8H_4ONCl_3$. Calculated %: Cl 44.03.

4-Cyanophenyl trifluoromethyl ether. 46.7 g 4-cyanophenyl trichloromethyl ether and 45 g antimony trifluoride were placed in a Wurtz flask, 2 ml antimony pentachloride added and the mixture heated to boiling. After several minutes the reaction product was distilled, together with the antimony trichloride. The product was extracted with ether and washed with 15% hydrochloric acid. The ethereal solution was dried and the ether distilled off. The products from three such experiments were combined and fractionated on a small column. Yield 22.5 g (20%). B.p. 192-192°.

Found %: N 7.18, 7.31. $C_8H_4ONF_3$. Calculated %: N 7.48.

4-Trifluoromethoxybenzamide. 1) A solution of 18.7 g 4-cyanophenyl trifluoromethyl ether in 75 ml alcohol was placed in a round-bottomed flask, followed by 6.5 ml 6N caustic soda and 65 ml 25% hydrogen peroxide. Oxygen was liberated from the mixture and the reaction became exothermic. The temperature was maintained at 40-50° with external cooling. When the evolution of heat had ceased, the solution was heated for 3 hours at 50°, neutralized to litmus with 5% sulfuric acid, cooled, and the crystals obtained separated and washed with water. 16.1 g of product (76.5%) was obtained after crystallization from aqueous alcohol. M.p. 150-151°. A second crystallization gave a product with m.p. 151-152°.

Found %: N 6.64, 6.66. $C_8H_6O_2NF_3$. Calculated %: N 6.83.

2) It is more convenient to prepare 4-trifluoromethoxybenzamide by the method described below.

Anisyl chloride. A mixture of 103 g anisic acid and 500 g thionyl chloride was boiled for 2 hours on the water bath. The product was distilled over. B.p. 106-107° (4 mm). Yield 100.5 g (87%). Literature data, b.p. 140-141° (14 mm) [4].

4-Trichloromethoxybenzoyl chloride. 100 g anisyl chloride was placed in a three-necked flask fitted with thermometer, reflux condenser and bubbler, 6.4 g phosphorus pentachloride added and dry chlorine passed through for 4 hours at 190-200° until the increase in weight was 95% of the theoretical calculated amount. The mixture was vacuum distilled. Two fractions were collected: 1st b.p. up to 138° (4 mm), 6 g; 2nd b.p. 138-140° (4 mm), 139.2 g (87%); the second fraction was fluorinated without further purification.

4-Trifluoromethoxybenzoyl fluoride. 105.9 g 4-trichloromethoxybenzoyl chloride, 105 g antimony trifluoride and 2.5 ml antimony pentachloride were placed in a Claisen flask. The mixture became hot and all the antimony trifluoride passed into solution. The product was distilled off in vacuo at the water pump and then separated from the antimony trichloride by fractionation on a small column at ordinary pressure. B.p. 161-162°. Yield 57 g (71%).

4-Trifluoromethoxybenzamide. 40.4 g 4-trifluoromethoxybenzoyl fluoride was placed in a reaction vessel cooled externally with ice, and 52 ml 25% ammonia solution added gradually with stirring. The mixture was stirred for 30 minutes and the precipitate filtered off and washed with water. After recrystallization from alcohol, 33.5 g (85%) of amide with m.p. 152-154° was obtained. A sample gave no melting point depression when mixed with the amide obtained from 4-cyanophenyl trifluoromethyl ether.

4-Aminophenyl trifluoromethyl ether. A solution of 33.3 g caustic potash in 280 ml water was placed in a reaction vessel fitted with thermometer and mechanical stirrer, the solution cooled to 0°, 4.9 ml bromine added, the mixture stirred and well-powdered 4-trifluoromethoxybenzamide sprinkled in immediately. The mixture was stirred at 0° until all the amide had passed into solution and then for 20 minutes at 75-80°. The amine was distilled off with steam and the distillate extracted with ether. The ether solution was dried, the ether distilled off and the amine vacuum distilled. B.p. 73-75° (10 mm). Yield 9.3 g (70%).

Found %: N 7.72, 7.76. $C_7H_6ONF_3$. Calculated %: N 7.91.

The liquid remaining after steam distillation of the amine was filtered through a folded filter and p-trifluoromethoxybenzoic acid (0.54 g) precipitated with hydrochloric acid. M.p. 150-151° (after two crystallizations from alcohol).

4-Acetylaminophenyl trifluoromethyl ether melted at 114-115°.

Found %: N 6.34, 6.50. $C_9H_8O_2NF_3$. Calculated %: N 6.39.

2-Methyl-6-trifluoromethoxybenzothiazole. A mixture of 4.2 g 4-acetylaminophenyl trifluoromethyl ether and 2.4 g phosphorus pentasulfide was ground up in a mortar and placed in a test-tube. This was heated on an oil bath to 115°, at which the mixture began to melt, and the temperature of the bath was then raised rapidly to 125°. After 1 minute the melt acquired a chocolate color. The test-tube was removed from the bath. The test-tube was cooled and broken and the contents dissolved in 70 ml 2N caustic soda and filtered. The thioacetyl derivative was precipitated from the alkaline solution with carbon dioxide, filtered and washed with water. Yield 2.2 g (50%).

2.2 g 4-thioacetylaminophenyl trifluoromethyl ether was dissolved with cooling in 50 mg 2N caustic soda and added dropwise with stirring to a solution of potassium ferricyanide (50 ml) which was cooled by ice. When

the solution had been mixed, stirring was continued for a further hour. The next day the yellow oil which had separated was extracted with ether, the ether solution washed with water, the ether distilled off and the residue steam distilled. The oil which distilled over solidified on cooling. The product was dissolved in hydrochloric acid (1 : 1). The solution was boiled with charcoal, filtered and neutralized with ammonia. Yield 1 g (45.4%). M.p. 56-57°. M.p. 57-58° after crystallization from aqueous alcohol.

Found %: N 6.05, 6.11. $C_9H_6ONSF_3$. Calculated %: N 6.00.

The ethyltosylates of 2-methyl-5- and 2-methyl-6-trifluoromethoxybenzothiazoles were prepared by heating 1 mole of the base with 1.2 mole of ethyl p-toluenesulfonate for 4 hours at 140-150°. The quaternary salts solidified on cooling and were washed with ether. The iodides were precipitated from aqueous solution with solid potassium iodide.

The dyes

I. 6, 6'-Bis-trifluoromethoxy-3, 3'-diethylthiacarbocyanine iodide. 0.22 g 2-methyl-6-trifluoromethoxybenzothiazole ethiodide, 0.22 g orthoformic ester and 2.5 ml pyridine were boiled for 45 minutes. The dye which precipitated was crystallized from alcohol. Yield 0.07 g (38%). Decomp. temp. 266-268°.

Found %: I 19.40, 19.42. $C_{23}H_{19}O_2N_2S_2IF_6$. Calculated %: I 19.24.

II. 5, 5'-Bis-trifluoromethoxy-3, 3'-diethylthiacarbocyanine iodide. Prepared as in the previous example. Long violet needles. Yield 44%. Decomp. temp. 268-269°.

Found %: I 19.11, 19.14. $C_{23}H_{19}O_2N_2S_2IF_6$. Calculated %: I 19.24.

III. 6, 6'-Bis-trifluoromethoxy-3, 3'-diethyl-9-methylthiacarbocyanine iodide. 0.2 g 2-methyl-6-trifluoromethoxybenzothiazole ethiodide, 0.2 g orthoacetic ester, 3 ml pyridine and 2 drops of acetic anhydride were boiled for 45 minutes. The dye which precipitated was crystallized from alcohol. Yield 0.05 g (29%). Decomp. temp. 265-266°.

Found %: I 18.93, 19.06. $C_{24}H_{21}O_2N_2S_2IF_6$. Calculated %: I 18.84.

IV. 5, 5'-Bis-trifluoromethoxy-3, 3'-diethyl-9-methylthiacarbocyanine iodide was prepared as in the previous example. Green needles, yield 35%. Decomp. temp. 265-266°.

Found %: I 18.86, 19.03. $C_{24}H_{21}O_2N_2S_2IF_6$. Calculated %: I 18.84.

V. 6, 6'-Bis-trifluoromethoxy-3, 3'-diethyl-9-ethylthiacarbocyanine iodide. 0.4 g 2-methyl-6-trifluoromethoxybenzothiazole ethyltosylate, 0.4 g orthopropionic ester, 2 ml pyridine and 3 drops of acetic anhydride were boiled for 10 minutes. The dye was precipitated with ether, dissolved in alcohol and converted to the iodide by addition of anaqueous solution of potassium iodide. Crystallized from alcohol. Yield 0.1 g (30%). Decomp. temp. 248-249°.

Found %: I 18.34, 18.40. $C_{25}H_{23}O_2N_2S_2IF_6$. Calculated %: I 18.17.

VI. 5, 5'-Bis-trifluoromethoxy-3, 3'-diethyl-9-ethylthiacarbocyanine iodide was prepared as in the previous example. Yield 37%. Decomp. temp. 237-238°.

Found %: I 18.44, 18.32. $C_{25}H_{23}O_2N_2S_2IF_6$. Calculated %: I 18.17.

VII. 2-p-Dimethylaminostyryl-6-trifluoromethoxybenzothiazole ethiodide. 0.2 g 2-methyl-6-trifluoromethoxybenzothiazole ethyltosylate, 0.08 g p-dimethylaminobenzaldehyde and 2 ml acetic anhydride were boiled for 45 minutes. The dye was precipitated with ether, converted to the iodide and the latter crystallized from alcohol. Yield 0.2 g (66%). Decomp. temp. 250-252°.

Found %: I 24.18, 24.47. $C_{20}H_{20}ON_2SIF_3$. Calculated %: I 24.42.

VIII. 2-p-Dimethylaminostyryl-5-trifluoromethoxybenzothiazole ethiodide. 0.1 g 2-methyl-5-trifluoromethoxybenzothiazole ethiodide and 0.08 g p-dimethylaminobenzaldehyde were boiled with 2 ml acetic anhydride for 30 minutes. The dye which precipitated was crystallized from alcohol. Yield 0.1 g (80%) Decomp. temp. 230°.

Found %: I 24.16, 24.26. $C_{20}H_{20}ON_2SIF_3$. Calculated %: I 24.42.

SUMMARY

A method has been worked out for the preparation of 4-aminophenyltrifluoromethyl ether.

A description is given of the synthesis of 2-methyl-5- and 2-methyl-6-trifluoromethoxybenzothiazoles. From their quaternary salts, 8 thiacarbocyanines, containing trifluoromethoxy groups in the 5 and 6 positions of the benzothiazole nucleus, have been prepared. It has been found that the absorption maxima of the thiacarbocyanines with the OCF_3 substituent are practically the same as the absorption maxima of the unsubstituted dyes.

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THE SYNTHESIS OF CERTAIN SUBSTITUTED HEXAHYDROPYRIMIDINES (PIPERIMIDINES)

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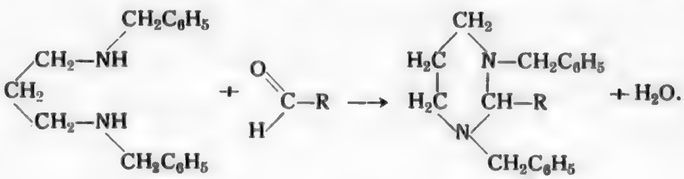
It is known that certain heterocyclic compounds containing a benzene residue are physiologically active materials. To this class of compound, for example, belong the alkaloid papaverine and the pharmaceutical preparations benzoline (2-benzylimidazoline) and dibasol (2-benzylimidazole). Active pyrimidine compounds containing the benzyl group have also been described [1].

In the present work we give the syntheses of hexahydropyrimidine compounds containing N-benzyl groups (I). (We suggest the name "piperimidine" for tetrahydropyrimidine,* by analogy with the name piperidine for hexahydropyridine. These compounds were obtained by us in almost quantitative yield by the reaction of N, N'-dibenzyltrimethylenediamine with aromatic aldehydes according to the scheme:



(I)

Lob [2] has used a similar method to prepare imidazoline compounds starting from N, N'-dibenzylethylenediamine.

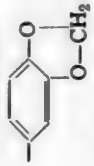
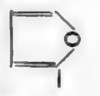
Only a few examples of the synthesis of piperimidine compounds have been described in the literature. Thus, Scholtz [3] prepared 1, 3-diphenylpiperimidine by the reaction of N, N'-diphenyltrimethylendiamine with formaldehyde; later, Scholtz and Jaross [4] prepared other piperimidines by reaction with acetaldehyde and propionaldehyde. There also exists a patent on the synthesis of piperimidines from propanediamine-1, 3 and aldehydes [5]. We have, however, found no references in the literature to 1, 3-dibenzyl derivatives of piperimidine, and even N, N'-dibenzylpropanediamine-1, 3, the starting material for the synthesis, does not appear to have been described.

The piperimidine compounds prepared by us are readily crystallizable substances; they have a constant melting point even after only one crystallization. They react as bases to form hydrochlorides and picrates. A characteristic reaction is the decomposition when heated with dilute acids, with the formation of the starting materials (diamine and aldehyde). In this respect the piperimidines obtained resemble the 1, 3-dibenzylimidazolidines described by Lob [2] and the 1, 3-diphenylimidazolines [6], which are also hydrolyzed to the aldehyde and diamine when heated in dilute acids.

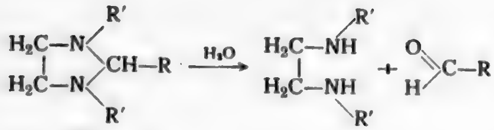
In the Table below we give the data for the piperimidines synthesized. We also give, for comparison, data on the analogous 1, 3-dibenzylimidazolidines (II R' = $CH_2C_6H_5$) (the imidazolidines prepared by us and not described in the literature are denoted by a slanting cross ×).

*As in original — Publisher's note.

TABLE

R in formulas (I) and (II)	Piperimidines (I) formula	melting point	N content (%) calc.	N content (%) found	1,3-Dibenzylimidazolidines (II, R' = $CH_2C_6H_5$) formula	melting point	N content (%) calc.	N content (%) found
C_6H_5	$C_{24}H_{26}N_2$	113—114°	8.18	8.52	$C_{23}H_{24}N_2$	98—99	8.32	8.32
C_6H_4Cl-p	$C_{24}H_{25}N_2Cl_2$	104—105	7.43 *	7.88	$C_{23}H_{23}N_2Cl$	109—110 (110) [2]	7.72	8.03
C_6H_4OH-o	$C_{24}H_{26}N_2O$	110—111	7.82	8.18	$C_{23}H_{24}N_2O$	107—108 (108) [2]	8.11	8.24
	$C_{25}H_{26}N_2O_2$	131—132	7.25	7.58	$C_{24}H_{24}N_2O_2$	112—113 (111—112) [2]	7.39	7.51
$C_6H_4NHCOCH_3$-p	$C_{26}H_{29}N_3O$	111—112	10.52	10.82	$C_{25}H_{27}N_3O$×	160—161	10.52	10.82
$C_6H_4N(CH_3)_2$-p	$C_{26}H_{31}N_3$	127—128	10.90	11.30	$C_{25}H_{29}N_3$ *×	121—122	11.32	11.51
	$C_{22}H_{24}N_2O$	71—72	8.43	8.81	$C_{21}H_{22}N_2O$	73—74 (74) [2]	9.80	8.87

* Found %: Cl 9.41. Calculated %: Cl 9.42.



(II)

$R' = CH_2C_6H_5,\ C_6H_5$.

EXPERIMENTAL

Dibenzylidenetrimethylenediamine. 24 ml 50% aqueous trimethylenediamine solution (0.164 mole) and 34.82 g (0.334 mole) freshly distilled benzaldehyde were placed in a round-bottomed flask with reflux condenser. The mixture was heated on an oil bath at 120° for half an hour. The azomethine obtained was extracted with ether. The ether extract was dried over ignited BaO, the ether distilled off and the azomethine vacuum distilled. Dibenzylidenetrimethylenediamine was obtained in the form of a colorless oil, b.p. 216-217° (5 mm). Yield 71 g (74%).

d_4^{20} 1.0403, n_D^{20} 1.596, MR_D 82.33; calc. 82.85.
Found %: N 10.89. $C_{17}H_{18}N_2$.
Calculated %: N 11.2

Picrate, m.p. 247-248°.

Found %: N 16.00. $C_{17}H_{18}N_2 \cdot 2C_6H_3N_3O_7$.
Calculated %: N 15.81.

N, N'-Dibenzyltrimethylenediamine. 68 g dibenzylidenetrimethylenediamine was dissolved in 700 ml anhydrous ethyl alcohol. 27.6 g metallic sodium was added portionwise to the solution over a period of 1.5 hours. When all the metallic sodium had been added, the reaction mass was cooled to room temperature and water added to decompose the alkoxide. This caused the diamine to separate on the surface in the form of an oily layer which was removed. To this was added concentrated hydrochloric acid. The hydrochloride which separated was recrystallized

from water. The salt was isolated in the form of colorless needles and melted at 288-289° (with decomp.).

Found %: N 8.76; Cl 21.44, 21.40. $C_{17}H_{22}N_2 \cdot 2HCl$. Calculated %: N 8.56; Cl 21.68.

The base was obtained by the addition of 30% NaOH solution to the purified hydrochloride. The base which separated was extracted with ether. The ether extract was dried with solid NaOH and then with BaO. The dried diamine was vacuum distilled. The fraction boiling at 201-203° (5 mm) was collected. The diamine had the form of a colorless oily liquid, rapidly becoming turbid in air as a result of absorption of carbon dioxide and formation of the carbonate. Yield 44.6 g (64.6%).

d_4^{20} 1.0211, n_D^{20} 1.562, MR_D 80.66; calc. 80.70.
Found %: N 10.8. $C_{17}H_{22}N_2$. Calculated %: N 11.02.

Picrate, m.p. 171-173°.

Found %: N 15.52. $C_{17}H_{22}N_2 \cdot 2C_6H_3N_3O_7$. Calculated %: N 15.73.

The synthesis of piperimidine derivatives. The piperimidine derivatives were prepared by mixing dibenzyltrimethylenediamine with aldehydes, using no solvent. The reaction took place with slight evolution of heat. When the aldehyde taken for the reaction was a liquid, the mixture of aldehyde and amine became turbid at first on mixing and after several minutes crystals of the piperimidine derivative came down. In the experiments with p-chlorobenzaldehyde and piperonal, the aldehyde was dissolved in the amine at room temperature and the corresponding piperimidine was precipitated in a few minutes. In the reaction with p-dimethylaminobenzaldehyde, the reaction mass had to be heated to 50°, to dissolve the aldehyde in the amine, after which 1, 3-dibenzyl-2-(p-dimethylaminophenyl)-piperimidine was soon precipitated.

As an example we give the synthesis of 1, 3-dibenzyl-2-(o-hydroxyphenyl)-piperimidine. 1 g N, N'-dibenzyltrimethylenediamine was mixed with 0.54 g salicylaldehyde. Slight evolution of heat was observed and the solution became turbid. After several minutes colorless crystals of the piperimidine were precipitated. Colorless plates, m.p. 110-111°, after recrystallization from alcohol. Soluble in alcohol, acetone, ether and benzene, insoluble in water. Yield 1.38 g (99%).

SUMMARY

1. The synthesis of N, N'-dibenzyldiaminopropane-1, 3 is described.

2. It has been shown that N, N'-dibenzyldiaminopropane-1, 3 reacts with aldehydes to give hexahydropyrimidine (piperimidine) derivatives in quantitative yield.

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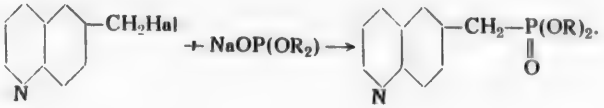
THE REACTION OF 6-MONOHALOGENOMETHYLQUINOLINES WITH SODIUM DIALKYL PHOSPHITES

B. P. Lugovkin

The synthesis of 6-chloro- and 6-bromethylquinolines [1] enables us to study their reaction with sodium dialkyl phosphites. V. S. Abramov and A. S. Kapustina have recently studied the reaction of dialkyl phosphites with 6-aldehydoquinoline; in this was they prepared esters of α-hydroxy-6-methylquinolinephosphinic(phosphonic) acid [2]. The reaction of ω-monohalogenomethylquinolines with esters of phosphorous acids has not been studied.

We have studied the reaction of 6-chloromethylquinoline with sodium dimethyl, diethyl, dipropyl and diisopropyl phosphites and of 6-bromomethylquinoline with sodium dibutyl and diisobutyl phosphite in absolute ether.

The reaction proceeded with the formation of esters of 6-methylquinolinephosphinic(phosphonic)acid according to the equation:



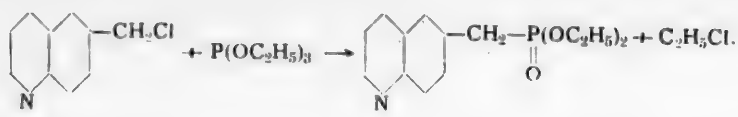
The esters obtained were thick liquids, soluble in water, alcohol and ether. They undergo considerable change on being heated to 130-200°.

The esters were isolated in the form of the picrates. The methiodides were also obtained. The results of the experiments are given in the Table.

R in ester formulae	Yield of ester as picrate (%)	Melting point		Picrate (%)		Methiodide (%)	
		Of picrate	Of methiodide	P found	P Calculated	I found	I Calculated
CH_3 . . .	21.0 *	161°	—	6.06	6.45	—	—
C_2H_5 . . .	73.5	156	111°	5.80	6.10	29.97	30.13
C_3H_7 . . .	52.5	127	Oily liquid	6.03	5.78	28.57	28.26
Iso -C_3H_7 .	54.0	161	130–131°	5.37	5.78	28.34	28.26
C_4H_9 . . .	60.0	134–135	Oily liquid	5.64	5.49	26.97	26.60
Iso -C_4H_9 .	64.0	135–136	108°	5.76	5.49	26.30	26.66

* The low yield of the dimethyl ester may be explained by the low solubility of sodium dimethyl phosphite in ether.

When 6-chloromethylquinoline was heated with triethyl phosphite at 130-135°, vigorous evolution of ethyl chloride took place according to the A. E. Arbuzov reaction:



Under the experimental conditions, however, the picrate and methiodide of the diethyl 6-methylquinolinephosphinate (phosphonate) could not be isolated.

EXPERIMENTAL

The preparation of diethyl 6-methylquinolinephosphinate (phosphonate). A solution of 6 g chloromethylquinoline in 35 ml dry ether was added to an ethereal solution of sodium diethyl phosphite (0.78 g metallic sodium in 40 ml dry ether and 4.7 g diethyl phosphite. The mixture was heated for 3 hours with the ether boiling.* The next day the precipitate of sodium chloride which had separated (1.9 g as against the 1.98 g required theoretically) was removed and washed with ether. The ether was distilled to yield 9.1 g of an oily liquid. When this was heated at 5 mm pressure and 200° (in Wood's metal), vigorous decomposition took place. In a repeat experiment the ester was isolated (without vacuum distillation) as the picrate.

The picrate was isolated in the form of yellow crystals with m.p. 156° by fractional crystallization from 1.3 g of the ester and 1.2 g picric acid in 10 ml anhydrous alcohol. Weight of picrate 1.8 g, which corresponds to 0.99 g diethyl 6-methylquinolinephosphinate (phosphonate).

The reaction of 6-chloro- and 6-bromomethylquinolines with the sodium salts of other dialkyl phosphites was carried out similarly.

The methiodides of the 6-methylquinolinephosphinic (phosphonic) esters were prepared by the action of methyl iodide (in excess) at ordinary temperatures for 3-4 days. The methiodides were heated with activated charcoal in anhydrous alcohol and precipitated with dry ether. Dark yellow oily liquids were obtained; some of them crystallized on standing. The methiodide of the diisobutyl ester was isolated in the form of pale yellow crystals. Yield of methiodides 70-80%. Readily soluble in water and anhydrous alcohol, insoluble in dry ether.

When ethyl 6-methylquinolinephosphinate (phosphonate) was hydrolyzed with dilute hydrochloric acid, 6-methylquinolinephosphinic (phosphonic) acid hydrochloride was obtained in the form of crystals with m.p. 286° (melted without sintering) (from aqueous alcohol).

SUMMARY

A study has been made of the reaction of 6-chloro- and 6-bromomethylquinolines with sodium dialkyl phosphites.

Dimethyl, diethyl, dipropyl, diisopropyl, dibutyl and diisobutyl 6-methylquinolinephosphinates (phosphonates) have been synthesized and identified as their picrates and methiodides.

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* In the experiments with 6-bromomethylquinoline the mixture was heated for half an hour; sodium bromide separated at ordinary temperatures.

** Original Russian pagination. See C. B. translation.

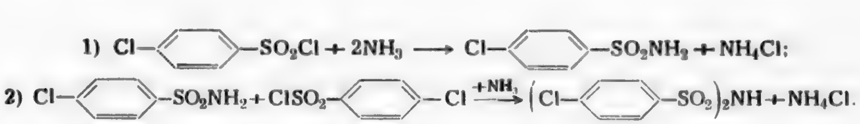
*** T. p. = C. B. Translation pagination.

p-CHLOROBENZENESULFONAMIDE AND ITS DERIVATIVES*

A. M. Grigorovsky, N. N. Dykhanov and Z. M. Kimen

There are in the literature very many examples, a number of which have been studied in detail, of the preparation of arylsulfonamides and their N-derivatives from arylsulfonyl chlorides. Certain of these reactions, which are of importance in connection with the preparation of medicinal compounds, have been less closely studied. In particular, it has proved necessary for production purposes to make a detailed study of the formation of p-chlorosulfonamide and its N-derivatives. These compounds may be used as intermediate products in the industrial synthesis of medicinal sulfanilamide materials.

The synthesis of p-chlorobenzenesulfonamide by the reaction of p-chlorobenzenesulfonyl chloride with aqueous ammonia solution was achieved at an early date; the first descriptions give no details and do not report the yield of amide [1]. This synthesis was repeated in 1947 by A. M. Grigorovsky and K. I. Znaeva; the yield of technical p-chlorobenzenesulfonamide obtained by them was more than 90% of the theoretical [2]. We have now established that the yield of p-chlorobenzenesulfonamide in the reaction of p-chlorobenzenesulfonyl chloride with aqueous ammonia solution, even when a large excess is used, may vary between wide limits, from 65 to 95% of the theoretical. The reason for this lies in the fact that in the above process, in addition to the main reaction involving the formation of the amide from the p-chlorobenzenesulfonyl chloride (1), a side reaction involving the acylation of the initially formed p-chlorobenzenesulfonamide by the p-chlorobenzenesulfonyl chloride (2) with the formation of the imide of p-chlorobenzenesulfonic acid (p-chlorobenzenesulfonimide):



p-Chlorobenzenesulfonimide is formed in minimum amount only with vigorous stirring of the reaction mass and slow addition of the sulfonyl chloride to the aqueous ammonia (to avoid local superheating). To achieve the best yield of p-chlorobenzenesulfonamide in the reaction of p-chlorobenzenesulfonyl chloride with aqueous ammonia solution, the reaction must be carried out by slowly adding 1 mole of the sulfonyl chloride to 4-5 moles of 17-25% ammonia solution at a temperature not exceeding 25° and with vigorous stirring. When the reagents have been mixed, the reaction mass must be heated for 50-60 minutes at 65-70°. Under these conditions the yield of p-chlorobenzenesulfonamide reaches 92-93% of the theoretical.

When stirring is inefficient and the sulfonyl chloride is added all at once, the yield of p-chlorobenzenesulfonamide falls sharply and the amount of imide formed reaches as much as 25% of the theoretically possible value.

In the reactions of benzenesulfonyl chloride and p-acylaminobenzenesulfonyl chlorides with ammonia in the same conditions, the corresponding imides, according to our observations, are not formed.

* Communication No. II in a series of works on the synthesis of sulfanilamide and its N-substituted derivatives; see [3] for communication No. I.

When all the sulfonyl chloride had been added, the reaction mass was slowly heated to 65-70° and kept at this temperature for 1 hour with uninterrupted stirring. The mixture of p-chlorobenzenesulfonamide, ammonium salt of p-chlorobenzenesulfonimide and p,p'-dichlorodiphenylsulfone which precipitated was filtered off, washed with 100 ml water and carefully pressed out. The moist paste of the mixed compounds (80-90 g) was added to 125 ml 10% aqueous caustic soda solution, stirred for 10 minutes and the part of the precipitate which did not dissolve — a mixture of p,p'-dichlorodiphenylsulfone and the sodium salt of p-chlorobenzenesulfonimide — filtered off. This mixture was washed on the filter with 25 ml 10% caustic soda solution and the washings added to the main filtrate.

The alkaline filtrate – a solution of the sodium salt of p-chlorobenzenesulfonamide – was acidified with concentrated hydrochloric acid until weakly acid to congo red. The precipitate of p-chlorobenzenesulfonamide obtained was filtered off, washed with water until the washings showed no acid reaction and dried to constant weight at 100°. The yield of p-chlorobenzenesulfonamide free from impurities amounted to 58-59 g (92-93%).

p-Chlorobenzenesulfonamide is readily soluble in alcohol, acetone, pyridine and in dilute aqueous solutions of caustic alkali, sparingly soluble in cold water (1:250) and also in aqueous alkali carbonate solutions; it crystallizes from water (1:25) in the form of fine colorless needles, m.p. 146-147°.

The mixture of p, p'-dichlorodiphenylsulfone and the sodium salt of p-chlorobenzenesulfonimide obtained as described above was added to 50-60 ml boiling water, stirred for 2-3 minutes and the water-insoluble p, p'-dichlorodiphenylsulfone filtered off; after recrystallization from 4 times its weight of acetone, the sulfone was obtained in the form of white needles, m.p. 147-148°. The yield of sulfone corresponds to the amount determined by analysis in the paste of the technical sulfonyl chloride (4-5 g).

The aqueous filtrate (from the separation of the p, p'-dichlorodiphenylsulfone) was evaporated to a volume of 20-25 ml. In this way a white crystalline precipitate was obtained, filtered off and dried at 105° to constant weight. 1.8-2.5 g of the sodium salt of p-chlorobenzenesulfonimide was obtained, which corresponds to 3-4% of the possible amount calculated on the p-chlorobenzenesulfonyl chloride taken for the reaction.

The sodium salt of p-chlorobenzenesulfonimide is insoluble in organic solvents; solubility in water at 20° – 1:200; crystallized from hot water (1:3) in the form of colorless plates, which remain unchanged when heated up to 250°.

Found %: C 37.46; H 2.01; N 3.67; Cl 18.34. $C_{12}H_8O_4NS_2Cl_2Na$. Calculated %: C 37.32; H 2.04; N 3.60; Cl 18.26.

The imide of p-chlorobenzenesulfonic acid, isolated from a solution of its sodium salt by neutralization with sulfuric or hydrochloric acid, is a white amorphous powder, melting after drying at 203-205°; readily soluble in the cold in alcohol, acetone, pyridine and in aqueous alkali carbonate solutions (in contrast to the corresponding amide); sparingly soluble in cold water (1:75 at 20°) and completely insoluble in aromatic hydrocarbons; crystallized from water (1:30) in the form of fine colorless needles, m.p. 207-208°.*

Found %: C 39.47; H 2.34; N 4.03; Cl 19.21. $C_{12}H_9O_4NS_2Cl_2$. Calculated %: C 39.31; H 2.47; N 3.82; Cl 19.36.

The structure of p-chlorobenzenesulfonimide is proved by its synthesis from p-chlorobenzenesulfonyl chloride and the sodium salt of p-chlorobenzenesulfonamide as described below. 500 ml 5% caustic soda solution and 21 g p-chlorobenzenesulfonamide were placed in an apparatus similar to that used for the preparation of the amide from p-chlorobenzenesulfonyl chloride. 38 g of a paste of 70% technical p-chlorobenzenesulfonyl chloride (containing 5.5% p, p'-dichlorodiphenylsulfone) was added in small portions with stirring at 48-50° to the solution obtained. The reaction medium was kept weakly alkaline to bromothymol blue (pH approximately 7) throughout this process by the periodic addition of 5% caustic soda solution to the reaction mass. When all the sulfonyl chloride had been added, the reaction mass was heated to 80°; after 10 minutes' stirring at this temperature the precipitate of p, p'-dichlorodiphenylsulfone was filtered off. The filtrate – a solution of the sodium salt of p-chlorobenzenesulfonimide – was clarified by boiling with activated charcoal; the solution was filtered from the charcoal, cooled to room temperature and 40% caustic soda solution added until no further precipitate came down (140-150 ml). The precipitate of the sodium salt of p-chlorobenzenesulfonimide obtained was filtered off, washed

* Literature data for this compound, m.p. 206-207° [11].

The presence in technical p-chlorobenzenesulfonyl chloride of p, p'-dichlorodiphenylsulfone impurity in amounts up to 8% by weight of the sulfonyl chloride* has no influence on the experimental result. On this basis we used both pure and technical p-chlorobenzenesulfonyl chloride in the synthesis of p-chlorobenzenesulfonamide and its derivatives. The alkali-insoluble p, p'-dichlorodiphenylsulfone was quantitatively separated (by filtration) from the solutions of the alkali salts of p-chlorobenzenesulfonamide and its N-monosubstituted derivatives.

The separation of the amide and imide of p-chlorobenzenesulfonic acid is easily achieved, thanks to their different solubilities in excess aqueous caustic alkali solution. The sodium salt of the imide, which is sparingly soluble in excess caustic soda, is separated together with the p, p'-dichlorodiphenylsulfone by filtration from the sodium salt of the amide, which is readily soluble under the same conditions. The sodium salt of the p-chlorobenzenesulfonimide is separated from the p, p'-dichlorodiphenylsulfone by dissolving in hot water; it is reprecipitated by concentrating the aqueous solution by evaporation. The amide and imide of p-chlorobenzenesulfonic acid are isolated by precipitation on neutralization of aqueous solutions of their sodium salts with sulfuric or hydrochloric acid. An aqueous solution of p-chlorobenzenesulfonimide, unlike that of p-chlorobenzenesulfonamide, gives a reaction with congo red similar to that of strong acids.

For the preparation of p-chlorobenzenesulfonamide derivatives containing aliphatic or unsubstituted aromatic radicals on the nitrogen, we successfully employed the method for the synthesis of such compounds proposed as early as 1870 by A. F. Wolkowa. According to this method, N-alkyl- and N-arylamides of arylsulfonic acids are prepared by the reaction of equimolecular amounts of arylsulfonyl chlorides and alkylamines (or arylamines) in the presence of an equivalent quantity of aqueous caustic alkali solution [4]. We have studied the reaction under these conditions of p-chlorobenzenesulfonyl chloride with ethylamine and aniline. The synthesis of p-[N-(p'-sulfonamidophenyl)]-chlorobenzenesulfonamide from p-chlorobenzenesulfonyl chloride and sulfanilamide cannot be achieved in this way, since, in this case, in the presence of caustic alkali, the sulfonic acid residue replaces a hydrogen atom in the N^1 position in the sulfanilamide [5]. A suitable method for the synthesis of the compound named above is that for the synthesis of N^4-(N-acylsulfanilyl) derivatives of sulfanilamide, proposed by E. S. Golovchinskaya and consisting of the alternate addition of acylanilylsulfonyl chloride and sodium carbonate to an aqueous solution of sulfanilamide saturated with sodium chloride and heated to 70° [6].

p-Chlorobenzenesulfonamide derivatives with heterocyclic nitrogen-containing radicals as substituents on the nitrogen were prepared by us by the reaction of equimolecular quantities of p-chlorobenzenesulfonyl chloride and primary heterocyclic amines in pyridine solution. The N-(2-pyridyl), N-(2-pyrimidyl) and N-(2-thiazolyl) derivatives of p-chlorobenzenesulfonamide have been prepared in this way. These compounds, like the above-mentioned p-N-(p'-sulfonamidophenyl)-chlorobenzenesulfonamide, cannot be prepared by the method of A. F. Wolkowa: 2-amino-substituted nitrogen-containing heterocyclic compounds react in aqueous alkaline medium in the tautomeric form with two molecules of arylsulfonyl chloride, with the formation of N, N'-disubstituted derivatives [7].

We have achieved the synthesis of several N-acyl derivatives of p-chlorobenzenesulfonamide by the action of acylating agents on the amide.

N-acyl derivatives of p-chlorobenzenesulfonamide have greater acidic properties than p-chlorobenzenesulfonamide: a characteristic reaction is the formation of metallic salts by merely dissolving in alkali carbonates. This property may be used to separate a mixture of p-chlorobenzenesulfonamide and its N-acyl derivative.

EXPERIMENTAL

The amide and imide of p-chlorobenzenesulfonic acid. 125 ml 25% aqueous ammonia solution was placed in a three-necked flask of 500 ml capacity fitted with stirrer and thermometer, and 110-120 g of a moist paste of technical p-chlorobenzenesulfonyl chloride containing by analysis** 70% basic material and 4-5 g p, p'-dichlorodiphenylsulfone was added in small portions over a period of 30-40 minutes. During the addition of the sulfonyl chloride the temperature of the reaction mass was kept between 20-25° by external cooling with water.

* p-p'-Dichlorodiphenylsulfone is formed in the amount indicated together with the p-chlorobenzenesulfonyl chloride in the reaction of chlorosulfonic acid with chlorobenzene [3].

** The method for the analysis of technical p-chlorobenzenesulfonyl chloride has been given earlier [3].

with 100 ml water, cooled to 5-6° and dried to constant weight at 105°; 41.6 g of dry salt was obtained (96.7% of the theoretically possible amount calculated on the p-chlorobenzenesulfonamide taken for the reaction). The free imide of p-chlorobenzenesulfonic acid, m.p. 207° (from water) was obtained from its sodium salt by the method described above. A mixture of this substance with the p-chlorobenzenesulfonimide obtained as a side-product of the preparation of the amide from p-chlorobenzenesulfonyl chloride melted without depression.

p-(N-Ethyl)-chlorobenzenesulfonamide. 75 ml 25% caustic soda solution and 150 g of a paste of technical 80% p-chlorobenzenesulfonyl chloride (0.57 mole) were added alternately in small portions with vigorous stirring to a solution of 24 g ethylamine (0.53 mole) in 280 ml water, the temperature being kept within the limits 35-40°. The mixture was stirred for 1 hour and then cooled to 20-25°. The mixture of p-(N-ethyl)-chlorobenzenesulfonamide and p, p'-dichlorodiphenylsulfone precipitated was filtered off and washed successively with 50 ml water, 5 ml 2% hydrochloric acid and again with water until the washings showed no acid reaction to congo red.

The technical p-(N-ethyl)-chlorobenzenesulfonamide was added to 2.5 liters 4% caustic soda solution and heated with stirring to 50°. The mixture was cooled, the alkali-insoluble p, p'-dichlorodiphenylsulfone filtered off, the filtrate clarified with charcoal and p-(N-ethyl)-chlorobenzenesulfonamide separated by the addition of 15% hydrochloric acid; the precipitate was filtered off, washed with water and dried. Yield 108.6 g (93% of the theoretical, calculated on the ethylamine). The substance is readily soluble in alcohol, acetone and ether, sparingly soluble in benzene and toluene, insoluble in water; crystallized from alcohol (1:5) in the form of colorless needles, m.p. 73.5°.

Found %: C 43.98; H 4.34; N 6.40. $C_8H_{10}O_2NSCl$. Calculated %: C 43.72; H 4.58; N 6.36.

p-(N-Phenyl)-chlorobenzenesulfonamide. Prepared as in the previous experiment from 66 g of a paste of technical 80% p-chlorobenzenesulfonyl chloride, 25 ml 25% caustic soda solution and an emulsion of 23.3 g aniline in 265 ml water; yield 95% of the theoretical.

p-(N-Phenyl)-chlorobenzenesulfonamide is readily soluble in the cold in alcohol, acetone and ether, insoluble in water, benzene and toluene; crystallizes from 50% alcohol in the form of colorless plates, m.p. 105° [8].

Found %: C 53.72; H 3.68; N 4.98. $C_{12}H_{10}O_2NSCl$. Calculated %: C 53.83; H 3.76; N 5.23.

p-[N-(p'-Sulfonamidophenyl)]-chlorobenzenesulfonamide. The synthesis of this compound from sulfanilamide and p-chlorobenzenesulfonyl chloride was carried out in conditions similar to those recommended for the preparation of the medicinal compound disulfane—N^4-sulfanilylsulfanilamide [6].

p-[N-p'-sulfonamidophenyl]-chlorobenzenesulfonamide was obtained with m.p. 186-188° (80-82% of theoretical, calculated on the sulfanilamide) after precipitation from alkaline solution. The substance is readily soluble in alcohol and acetone, insoluble in water, dichloroethane and aromatic hydrocarbons; crystallizes from 50% alcohol in the form of colorless leaflets, m.p. 196-196.5°.

Found %: N 7.88; Cl 10.31. $C_{12}H_{11}O_4N_2S_2Cl$. Calculated %: N 8.07; Cl 10.22.

p-[N-(2-Pyridyl)]-chlorobenzenesulfonamide. According to patent data, p-[N-(2-pyridyl)]-chlorobenzenesulfonamide and the p-[N (2-thiazolyl)]-chlorobenzenesulphonamide described below can be prepared by heating p-chlorobenzenesulfonamide with 2-bromopyridine and 2-bromothiazole respectively in the presence of copper catalyst and substances which combine with the hydrogen chloride liberated [9]. The properties of neither substance are described in the patents. The compounds named were prepared by us by the reaction of p-chlorobenzenesulfonyl chloride with 2-aminopyridine and with 2-aminothiazole in pyridine solution.

152 g technical p-chlorobenzenesulfonyl chloride (0.5 mole) was added in small portions with stirring to a solution of 47 g 2-aminopyridine (0.5 mole) in 300 ml pyridine. The reaction mass was then heated for 3 hours at 65-70°, after which 150 ml of pyridine was distilled off.

The part of the reaction mass remaining was poured with stirring into 5 times its volume of water. The mixture of p-[N-(2-pyridyl)]-chlorobenzenesulfonamide and p, p'-dichlorodiphenylsulfone precipitated in this way was filtered off, washed carefully with water and then heated with 200 ml 8% aqueous caustic soda solution for 10-15 minutes at 50°. The alkali-insoluble p, p'-dichlorodiphenylsulfone was filtered off; the filtrate—a solution of the sodium salt of p-[N-(2-pyridyl)]-chlorobenzenesulfonamide—was clarified by boiling with active charcoal and the free p-[N-(2-pyridyl)]-chlorobenzenesulfonamide isolated from it in the form of a light cream-colored precipitate by the addition of concentrated hydrochloric acid until weakly acid to congo red. The precipitate of

the amide was filtered off, washed with water and dried at 150°; a material with m.p. 188-190° was obtained, yield 100-101 g (74-75%).

p-[N-(2-Pyridyl)]-chlorobenzenesulfonamide is readily soluble in alcohol, acetone and pyridine, insoluble in water and in aromatic hydrocarbons; crystallizes from alcohol (1:5) in the form of fine colorless needles, m.p. 191-191.5°.

Found %: N 10.65; Cl 13.00. $C_{11}H_9O_2N_2SCl$. Calculated %: N 10.42; Cl 13.19.

p-[N-(2-Pyrimidyl)]-chlorobenzenesulfonamide. 11.5 g 2-aminopyrimidine (0.12 mole), 46 g technical p-chlorobenzenesulfonyl chloride (0.19 mole) and 75 ml pyridine were heated for 30 minutes at 50°. The amide was purified as in the previous synthesis. Yield of technical p-[N-(2-pyrimidyl)]-chlorobenzenesulfonamide with m.p. 200-203° – 21 g (65%).

The substance dissolves on heating in ethyl alcohol, acetone and pyridine, is insoluble in water, methyl alcohol and aromatic hydrocarbons; crystallizes from a mixture of acetone and methyl alcohol in the form of colorless needles, m.p. 203-204°.

Found %: C 44.54; H 3.00; N 15.36. $C_{10}H_8O_2N_3SCl$. Calculated %: C 44.53; H 2.98; N 15.58.

p-[N-(2-Thiazolyl)]-chlorobenzenesulfonamide. The mixture of p-[N-(2-thiazolyl)]-chlorobenzenesulfonamide and p, p'-dichlorodiphenylsulfone obtained by heating 50 g technical 89.7% 2-aminothiazole with 160 g technical 67% p-chlorobenzenesulfonyl chloride in 125 ml pyridine for 4 hours at 70-80° was diluted with 200 ml water and the precipitate obtained treated with 150 ml aqueous caustic soda solution as described above for the similar operation in the synthesis of p-[N-(2-pyridyl)]-chlorobenzenesulfonamide.

In this way 37 g (~27%) of p-[N-(2-thiazolyl)]-chlorobenzenesulfonamide with m.p. 198-200° was obtained. The substance is readily soluble in alcohol, acetone and pyridine, insoluble in water and aromatic hydrocarbons; crystallizes from alcohol (1:5) in the form of fine colorless needles, m.p. 201-202°.

Found %: N 10.30; Cl 12.69. $C_9H_7O_2N_2S_2Cl$. Calculated %: N 10.19; Cl 12.90.

p-(N-Benzoyl)-chlorobenzenesulfonamide. This compound was synthesized by N. V. Khromov-Borisov by heating 1 mole p-chlorobenzenesulfonamide with 2.5 moles benzoyl chloride at 160-200° [10]. We carried out the benzoylation of p-chlorobenzenesulfonamide with an excess of benzoyl chloride in aqueous caustic alkali solution.

154 g benzoyl chloride was added with stirring over a period of 2.5-3 hours to a solution of 191.5 g p-chlorobenzenesulfonamide in 950 ml 5% caustic soda solution. The reaction medium was kept weakly alkaline to bromothymol blue by the addition of small portions of 5% caustic soda solution (700-701 ml in all). The reaction solution was clarified with charcoal; the charcoal was filtered off and the p-(N-benzoyl)-chlorobenzenesulfonamide liberated by the addition of 15 % hydrochloric acid; the amorphous precipitate was filtered off, washed with water and dried. Yield 285 g (96%). The substance is sparingly soluble in cold water; solubility in hot water – 1:40; it dissolves in alcohol, acetone and pyridine; crystallizes from 50% alcohol in the form of colorless needles, m.p. 182°.

Found %: N 4.74; Cl 12.05. $C_{13}H_{10}O_3NSCl$. Calculated %: N 4.72; Cl 11.94.

p-(N-Acetyl)-chlorobenzenesulfonamide. A solution of 360 g p-chlorobenzenesulfonamide and 280 g acetic anhydride in 525 ml dry pyridine was boiled gently for 3 hours and then poured with stirring into 3 liters of cold water. The precipitate obtained was filtered off, carefully washed with water and dried at 105°. Yield of p-(N-acetyl)-chlorobenzenesulfonamide, m.p. 186-189°, 395 g (90% of theoretical, calculated on the chlorobenzenesulfonamide).

The substance is sparingly soluble in cold water; its solubility in boiling water is 1:30; it is readily soluble in the cold in dilute aqueous solutions of caustic alkali or alkali carbonates, in alcohol, acetone and pyridine; it does not dissolve in aromatic hydrocarbons; it crystallizes from 50% alcohol in the form of fine colorless needles, m.p. 192.5°.

Found %: N 5.91; Cl 15.28. $C_8H_8O_3NSCl$. Calculated %: N 5.98; Cl 15.17.

SUMMARY

1. In the reaction of p-chlorobenzenesulfonyl chloride with aqueous ammonia solution, there takes place, together with the main reaction, a side reaction involving the acylation of the initially formed p-chlorobenzenesulfonamide by the p-chlorobenzenesulfonyl chloride, as a result of which the imide of p-chlorobenzenesulfonic acid is formed. This side reaction may be almost completely avoided by mixing the reagents slowly with vigorous stirring.

2. In the synthesis of N-substituted derivatives of p-chlorobenzenesulfonamide by the reaction of p-chlorobenzenesulfonyl chloride with amines, decomposition of the amines may be decreased by using different bases which combine with the hydrogen chloride formed during the reaction. The choice of base in each case is determined by the properties of the original amine.

3. Derivatives of p-chlorobenzenesulfonamide containing the following radicals on the nitrogen have been described for the first time: C_2H_5, $C_6H_4SO_2NH_2$, $COCH_3$ and $C_4H_3N_2$ (pyrimidyl).

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THE AUTOXIDATION OF SUBSTITUTED ALKYL HOMOLOGS OF BENZENE

I. THE PREPARATION OF p-NITROCUMENE HYDROPEROXIDE

P. G. Sergeev and A. M. Sladkov

In a recently published work [1] Hock and Kropf mention the preparation by them of p-nitrocumene hydroperoxide by the autoxidation of p-nitrocumene. This report has led us to publish a small part of a study carried out by us some time ago on the autoxidation of alkyl homologs of benzene with substituents in the nucleus, namely the part devoted to the preparation and some of the reactions of p-nitrocumene hydroperoxide.

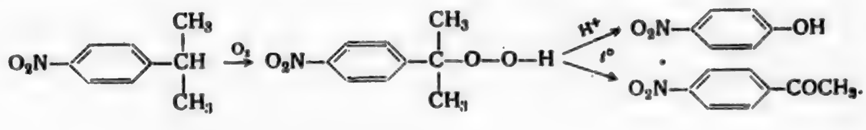
Whereas there is a great amount of data in the literature on the autoxidation of alkyl homologs of benzene [2] containing one or several alkyl groups, there are only isolated examples of the autoxidation of such compounds containing any sort of substituent in the nucleus. At the same time, as a rule, the primary products of the autoxidation–hydroperoxides–have not been isolated or studied, and the authors have based their conclusions on the course of the reaction solely from the final products.

Examples of these works include the study carried out by Emerson and coworkers [3] on the catalytic oxidation in the liquid phase of o- and p-nitroethylbenzenes to the corresponding nitroacetophenones, a short communication from Treves [4] on the autoxidation of 2-methoxy-2-nitrotoluene, a description of a method for the preparation of p-acetylbenzoic acid by the autoxidation of methyl p-ethylbenzoate [5], and finally, a report on the setting up of an industrial method for the preparation of terephthalic acid, one of the stages of which is the autoxidation of methyl p-toluate to mono-methyl terephthalate [6]. The last example shows the great importance of the study of the autoxidation of alkyl homologs of benzene with substituents in the nucleus.

It should be noted that the autoxidation of the compounds enumerated above was carried out, as a rule, in severe conditions (at 130-140°, in the presence of large quantities of catalyst), which leads to an abundance of side reactions and the complete decomposition of the hydroperoxides initially formed.

In contrast to these works, our aim has been to isolate the primary products of the autoxidation and to identify them by conversion of the hydroperoxides into known products by several reactions.

The reactions carried out by us, with p-nitrocumene as starting material, may be represented by the following scheme:



EXPERIMENTAL

The original p-nitrocumene was prepared by the nitration of isopropylbenzene with a mixture of nitric (d 1.4) and sulfuric (d 1.84) acids. Yield of p-nitrocumene with b.p. 107° (at 1 mm) approximately 80% n_D^{22} 1.5341, d_4^{22} 1.0900. Literature data [7]: n_D^{20} 1.53465, d_4^{20} 1.0852; b.p. 128.3° (at 12.8 mm).

The autoxidation of p-nitrocumene. The process was carried out in a glass column packed with segments of glass tubing 5 × 2 mm. Air was blown at a rate of 0.6-0.7 liters/minute through 50 ml (54.5 g; 0.33 mole) p-nitrocumene at 100°. 0.01 g nickel benzoate was added to initiate the process. After 55 hours the reaction mass contained 38.5% hydroperoxide (iodometric determination) and the refractive index of the reaction mass had risen to n_D^{22} 1.5540.

Isolation of the hydroperoxide. After the oxidation, an equal volume of n-pentane, with which p-nitrocumene is completely miscible, was added to the reaction mass. The part which was insoluble in the pentane had the form of a light yellow oil and gradually crystallized. The crystals were washed three times with pentane and then cooled to −5° with ether. 15.5 g of white crystalline material with m.p. 40-41° was obtained; m.p. 42° after recrystallization from ether (according to [1], m.p. 41°). Iodometric titration indicated that the specimen contained 98.9% hydroperoxide.

Found %: N 7.18. $C_9H_{11}O_4N$. Calculated %: N 7.09.

On prolonged standing in the light under normal conditions the hydroperoxide gradually became yellow and the crystals stuck together. When heated to 150-160° the hydroperoxide decomposed with spluttering and the evolution of soot.

Acid decomposition of the hydroperoxide. Approximately 2 g of the hydroperoxide obtained was dissolved in benzene (50 ml). 1 drop of concentrated sulfuric acid was then added with cooling to 0° and stirring. The mixture was gradually heated to room temperature with stirring and then stirred at 50-60° for 2 hours. Approximately 20 ml benzene was distilled from the reaction mass. The crystals which precipitated melted at 114° after recrystallization from toluene. When a sample was mixed with pure p-nitrophenol no melting point depression was obtained.

Thermal decomposition of the hydroperoxide. Approximately 2 g of the hydroperoxide obtained was dissolved in 50 ml tert-butylbenzene and the solution heated for 16 hours at 120-130°. The tert-butylbenzene was distilled off in vacuo at the water pump; the crystalline residue was recrystallized from acetone; melting point of substance isolated 81°. Literature data [8] for p-nitroacetophenone: m.p. 80-81°.

SUMMARY

p-Nitrocumene hydroperoxide has been prepared by the autoxidation of p-nitrocumene and identified by conversion to p-nitrophenol and p-nitroacetophenone.

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THE AUTOXIDATION OF SUBSTITUTED ALKYL HOMOLOGS OF BENZENE

II. THE PREPARATION OF p-ACETYLCUMENE HYDROPEROXIDE

P. G. Şergeev and A. M. Sladkov

A report in the literature [1] on the inhibiting action of the acetyl group in the autoxidation of p-ethylacetophenone led us to study the possibility of carrying out the autoxidation of certain p-acetyl derivatives of alkyl homologs of benzene. We chose, as the first compound for study, p-acetylcumene, since the presence of the isopropyl group attached to the benzene nucleus should make it possible to establish easily, in the autoxidation process, the presence of a hydroperoxide which is comparatively more stable than, for example, in the case of p-methyl or p-ethylacetophenone. At the same time this has made it possible for us to make a comparison with the autoxidation of cumene under the same condition.

As the experimental results have shown, the presence of the acetyl group in the para-position relative to the isopropyl group in p-acetylcumene not only does not show an inhibiting action, but even shows a slight accelerating influence on the formation of the hydroperoxide.

The p-acetylcumene hydroperoxide obtained in the autoxidation process was isolated and converted for identification to p-acetylphenol and p-diacetylbenzene according to the scheme given by us in an earlier communication [2] for p-nitrocumene.

EXPERIMENTAL

The original p-acetylcumene was obtained by the acetylation of isopropylbenzene with acetic anhydride in the presence of aluminum chloride. Yield of p-acetylcumene with b.p. 100° (3 mm) 89% n_D^{19} 1.5160, d_4^{19} 0.9554. Melting point 2, 4-dinitrophenylhydrazone 185°. (According to the literature data [3]: m.p. 185-186°).

The autoxidation of p-acetylcumene. The reaction was carried out in a glass column of 25 mm diameter packed with pieces of glass tubing 5 × 2 mm. Air was passed at a rate of 0.6-0.7 liters/minute through 60 ml (57.3 g; 0.3 mole) p-acetylcumene at 110° in the presence of 0.01 g nickel benzoate. After 9.5 hours, 27.5% hydroperoxide was found in the reaction mass (iodometric determination). In the autoxidation of cumene in the same conditions the hydroperoxide content after 8 hours amounted to 22.8%.

Isolation of the hydroperoxide. The reaction mass after the oxidation was added with vigorous stirring to a cooled mixture of ice and salt and 10% aqueous caustic soda solution (200 ml). The oil was separated from the alkaline layer, the alkaline solution was extracted with ether (5 times with 20 ml) and a current of carbon dioxide was then passed through it at 0° until the solution was fully saturated. The oily material which separated was extracted with ether (5 times with 15 ml), the combined ether extracts were dried with anhydrous sodium sulfate and the ether distilled off in vacuo. 10.2 g of a viscous light yellow liquid was obtained, containing 98.2% hydroperoxide (iodometric estimation). A second purification via the sodium salt raised the hydroperoxide content to 98.9% (iodometric estimation). n_D^{22} 1.5433, d_4^{22} 1.0930. MR_D 55.94; calc. 53.41.

When an attempt was made to carry out a vacuum distillation (1 mm) the hydroperoxide decomposed (at 160° in the bath).

Acid decomposition of the hydroperoxide. Approximately 1.5 g of the hydroperoxide obtained was dissolved in benzene (25 ml). The solution was cooled to 0° and 5 drops of 2% sulfuric acid added with stirring. The mixture was gradually heated with stirring to room temperature and then stirred on the water bath under reflux for

1.5 hours. The solvent was distilled completely from the reaction mass at low pressure and the residue recrystallized twice from a mixture of alcohol and benzene (1:1). A substance was obtained with m.p. 108-109°. Literature data for p-hydroxyacetophenone [4]: m.p. 109°.

Thermal decomposition of the hydroperoxide. Approximately 2.5 g of the hydroperoxide obtained was sealed in an atmosphere of nitrogen in an ampoule, which was then placed in an oil bath where it was kept at 120-135° for 20 hours. The ampoule was cooled and opened, the products of the thermal decomposition were washed with ether, cooled to 0° and then recrystallized twice from aqueous methanol (1:2). M.p. 112-113°. Literature data [5] for p-diacetylbenzene: m.p. 113°.

SUMMARY

1. It has been shown, in contradiction of the literature data, that the presence of the acetyl group in the para-position to the alkyl group in the benzene nucleus does not have an inhibiting action on the autoxidation.

2. p-Acetylcumene has been oxidized by atmospheric oxygen in the liquid phase to yield the corresponding hydroperoxide, which has been converted for identification to p-hydroxyacetophenone and p-diacetylbenzene.

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THE SYNTHESIS OF HARMINE DERIVATIVES. I.

N. I. Koretskaya, A. V. Danilova and L. M. Utkin

In the present article a description is given of the synthesis of certain harmine derivatives prepared for pharmacological studies.

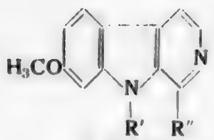
It has been established by the work of Perkin, Robinson and coworkers [1, 2] that in the action of alkyl halides on harmine the first stage is the reaction of the nitrogen of the pyridine nucleus with the formation of Py-N-alkyl derivatives which are capable, under the influence of alkali, of conversion to compounds of the anhydrobase type. When the latter are alkylated, the radical replaces the hydrogen of the indole nitrogen. It is also known that compounds of the indole series are capable of replacing the hydrogen on the nitrogen by potassium, by boiling with caustic potash in xylene [3]. We have used this reaction for the preparation of a number of derivatives.

We have prepared Ind-N-(β-diethylamino)-ethylharmine (I) by the action of diethyl-(β-chloroethyl)-amine on the potassium derivative of harmine. Harmine Py-N-(β-diethylamino)-ethyl chloride (II) was synthesized from harmine and diethyl-(β-chloroethyl)-amine. In anhydrous alcohol the yield of the hydrochloride of (II) amounted to 35%, in xylene—88% and in isopropyl alcohol—96.3%. The alkylation of Py-N-methylharmine [2] with diethyl-(β-chloroethyl)-amine was carried out in anhydrous alcohol and in a mixture of xylene and nitrobenzene (1:1) at their boiling points. In both cases, however, the original methylharmine was recovered.

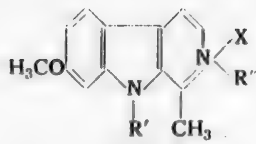
Acting on a suggestion that alkyl derivatives of tetrahydroharmine [4] may have interesting pharmacological properties, we prepared Py-N-(β-diethylamino)-ethyltetrahydroharmine (III) and carried out experiments on the preparation of Ind-N-benzyl-Py-N-methyltetrahydroharmine. Ind-N-benzylharmine (IV) was synthesized by the action of benzyl chloride on the potassium derivative of harmine. The yield of the hydrochloride of (IV) varied between 34 and 55%, depending on the degree of subdivision of the starting material. The preparation of Ind-N-benzylharmine Py-N-methiodide (V) was carried out with a good yield.

An attempt was then made to reduce Ind-N-benzylharmine Py-N-methiodide (V) with sodium in anhydrous alcohol in a current of nitrogen, but a tar was formed. The reduction of harmine methosulfate [2] was likewise unsuccessful using sodium in anhydrous alcohol, zinc dust in dilute acetic acid, platinum in anhydrous alcohol and in glacial acetic acid at 80°. In all the experiments the starting material was recovered unchanged. It follows from this that Py-quaternary derivatives of harmine are not reduced in the conditions described. As a result of the difficulties encountered in carrying out the reduction, we tried to prepare Ind-N-benzyl-Py-N-methyltetrahydroharmine by alkylation of tetrahydroharmine. In the methylation of tetrahydroharmine by Wallach's method, however, complete tar formation took place.

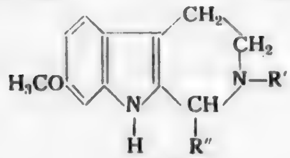
In view of the fact that esters of nor-harminecarboxylic acid may be of interest as intermediate products for the synthesis of medicinal products, experiments on their preparation were carried out. Nor-harminecarboxylic acid was prepared according to the method of Perkin and Robinson [5]. It is interesting to note that the melting point of the nor-harminecarboxylic acid obtained by us (237-238°) differs from that given in the work cited (258°); the analysis, however, corresponds to its elementary composition. The hydrolysis of ethyl nor-harminecarboxylate (VII) was carried out. The acid obtained by the hydrolysis had m.p. 237-238°. As a result of the low solubility of nor-harminecarboxylic acid, its esterification proceeds with low yields. When the esterification was carried out with diazomethane, via the chloride, via the potassium salt, ethylsulfuric acid and by the Fischer method, the best yields were obtained using the last method. The formation of esters of tetrahydro-nor-harminecarboxylic acid (VIII), prepared by the reduction of nor-harminecarboxylic acid, also proceeds with good yields.



(I, IV, VII)



(II, V, VI)



(III, VIII)

EXPERIMENTAL

Ind-N-(β-diethylamino)-ethylharmine (I), dihydrochloride. 5 g harmine and 1.4 g KOH (ground to powder) in 75 ml xylene were boiled under reflux with stirring for 3 hours. 3.25 g diethyl-(β-chloroethyl)-amine and 25 ml xylene were added to the reaction mixture and heating continued with stirring for a further 3 hours. The unreacted harmine was filtered off. The mother solution was evaporated in vacuo, the residue dissolved in 25 ml ether and an alcoholic solution of HCl added. 6.8 g (75.1%) of the dihydrochloride of (I), m.p. 270-271° (with decomp.) was obtained. The substance crystallizes from a mixture of methanol and ethanol (1 : 1).

Found %: C 57.05; H 7.46; N 10.20; Cl 17.78. $C_{19}H_{25}ON_3 \cdot 2HCl \cdot H_2O$. Calculated %: C 56.71; H 7.26; N 10.44; Cl 17.63.

Harmine Py-N-(β-diethylamino)-ethyl chloride (II), hydrochloride. 5 g harmine and 3.25 g dry, freshly distilled diethyl-(β-chloroethyl)-amine in 100 ml isoamyl alcohol were boiled under reflux for 3 hours. The solvent was distilled off in vacuo. The residue was dissolved in 15 ml methanol. 8.73 g (96.3%) of the hydrochloride of (II), m.p. 252-253°, was obtained by the addition of an alcohol solution of HCl; the substance crystallizes from a mixture of methanol and ethanol (1 : 1). The hydrochloride of (II) is readily soluble in water and methanol, less readily in ethanol. Dilute alcoholic solutions show fluorescence.

Found %: C 56.28; H 7.21; N 10.31; Cl 17.43. $C_{19}H_{26}ON_3Cl \cdot HCl \cdot H_2O$. Calculated %: C 56.71; H 7.26; N 10.44; Cl 17.63.

Py-N-(β-diethylamine)-ethyltetrahydroharmine (III). 1.6 g tetrahydroharmine and 1 g diethyl-(β-chloroethyl)-amine in 25 ml anhydrous alcohol were boiled for 1 hour under reflux. The alcohol was distilled off in vacuo. The residue was dissolved in water, made alkaline with 5% NH_4OH and extracted with ether. The ether extract was washed with water and the ether distilled off. The crystalline residue (1.55 g) had m.p. 96-116°.

1.23 g of the substance obtained was dissolved in 30 ml chloroform and passed through a column with 30 g Al_2O_3. The column was eluted successively with chloroform, a mixture of chloroform and methanol, and methanol. 1 g (54.0%) of (III) was isolated from the chloroform fractions; m.p. 95-97°; the substance was recrystallized from aqueous ether. A small quantity of tetrahydroharmine was washed out with the methanol. (III) crystallizes from water, decomposes in vacuo at 60°; turns yellow in air.

Found %: C 68.51, 68.36; H 9.22, 9.29; N 12.21, 12.19. $C_{19}H_{29}N_3O \cdot H_2O$. Calculated %: C 68.43; H 9.37; N 12.60.

With an alcoholic solution of picric acid, (III) gives a picrate with m.p. 186-187° (from acetone).

Ind-N-benzylharmine (IV). 5 g of powdered harmine and 2 g KOH (ground to a powder) in 80 ml xylene were boiled for 3 hours with stirring. 3 g of freshly distilled benzyl chloride was added and the reaction continued

for a further 3 hours. The undissolved residue (a mixture of unreacted harmine and KOH) was removed and the filtrate evaporated in vacuo. Concentrated HCl was added to the residue. 3.16 g (39.5%) of the hydrochloride of (IV) with m.p. 244-244.5° (from a mixture of acetone and methanol 1:1) was isolated by grinding with acetone.

Found %: Cl 10.43, 10.48. $C_{20}H_{18}ON_2 \cdot HCl$. Calculated %: Cl 10.46.

(IV) was isolated from the hydrochloride with 10% NH_4OH in the presence of ether; m.p. 133-134° after recrystallization from 75% methanol.

Found %: C 79.47; H 6.18; N 9.25. $C_{20}H_{18}ON_2$. Calculated %: C 79.44; H 6.00; N 9.27.

Ind-N-benzylharmine Py-N-methiodide (V). 0.75 g of (IV) and 1 g CH_3I in 10 ml methanol were heated under reflux on a water bath for 3 hours. The precipitate contained 0.99 g (90%) of (V); m.p. 265-267° (from methanol); sparingly soluble in water and alcohol.

Ind-N-benzylharmine Py-N-methyl chloride (VI). 4.8 g of (V) and freshly precipitated silver chloride (from 4 g $AgNO_3$) in 300 ml alcohol were shaken together at room-temperature for 5 hours. The mixture was then heated to 80° on the water bath and the AgI filtered off and washed with alcohol. The filtrate was evaporated in vacuo. 3.57 g (93.7%) of (VI) with m.p. 243-244° (from water) was isolated from the residue after the addition of 10 ml water.

Found %: Cl 9.20, 9.29. $C_{21}H_{21}ON_2Cl \cdot H_2O$. Calculated %: Cl 9.56.

Ethyl nor-harminecarboxylate (VII). A suspension of 2 g nor-harminecarboxylic acid in 40 ml anhydrous alcohol was saturated with gaseous HCl with cooling and then boiled for 6 hours under reflux on a water bath. This operation was repeated twice. The residue contained unreacted nor-harminecarboxylic acid (1 g). The filtrate was evaporated in vacuo, made alkaline and extracted with ether. A yellow oil which gave 0.78 g (30.8%) of crystalline hydrochloride was obtained from the ether. The compound (VII) was isolated from the hydrochloride with 10% NH_4OH in the presence of ether; m.p. 132-133° (from aqueous acetone).

Found %: C 66.94; H 5.26; N 10.28. $C_{15}H_{14}O_3N_2$. Calculated %: C 66.65; H 5.22; N 10.37.

The ester (VII) was hydrolyzed at 20° with 0.5N alcoholic alkali. The acid obtained, m.p. 237-237.5° (from glacial acetic acid), gave no melting point depression when mixed with nor-harminecarboxylic acid.

Tetrahydro-nor-harminecarboxylic acid (VIII). 2 g nor-harminecarboxylic acid in 250 ml anhydrous alcohol was reduced with 24 g Na at the boil. The solution was diluted with 200 ml water, the main bulk of the alcohol distilled off in vacuo and the reaction mass acidified with 90 ml HCl (1:1). The crystals which precipitated (1.7 g) were dissolved in 5% alcoholic alkali and neutralized with glacial acetic acid to pH 7-6.5 to yield 1.14 g (55.9%) of (VIII) with m.p. 200.5-201°.

Found %: C 63.36; H 5.73; N 11.19. $C_{13}H_{14}O_3N_2$. Calculated %: C 63.40; H 5.73; N 11.38.

SUMMARY

1. The following new derivatives of harmine have been synthesized: Ind-N-(β-diethylamino)-ethylharmine, dihydrochloride; harmine Py-N-(β-diethylamino)-ethyl chloride, hydrochloride; Ind-N-benzylharmine; Ind-N-benzylharmine Py-N-methiodide; Ind-N-benzylharmine Py-N-methyl chloride; ethyl nor-harminecarboxylate.

2. The following new derivatives of tetrahydroharmine have been prepared: Py-N-(β-diethylamino)-ethyltetrahydroharmine; tetrahydro-nor-harminecarboxylic acid.

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